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THE TREPHINE IN CHRONIC GLAUCOMA . T. HARRISON BUTLER

HISTOLOGY OF THE CORNEOSCLERAL MARGIN KAZUO HIWATARI

ASTIGMATISM—THE INFLUENCE OF AGE . . A. W. STIRLING

EYE DISEASE IN SYPHILIS AND TRYPANOSOMIASIS J. N. ROY

SYMPATHETIC OPHTHALMIA—A CASE SUCCESSFULLY TREATED ALFRED WIENER AND ELLIS BONIME

CYCLOPIA AND TERATOGENESIS (*Concluded*) . . . . EMORY HILL

DISCUSSION OF PERIMETRIC METHODS (*Oxford Congress*) P. G. DOYNE

REPORT OF THE PROCEEDINGS OF THE SECTION ON OPHTHALMOLOGY OF THE NEW YORK ACADEMY OF MEDICINE . . . . . CONRAD BERENS, JR.

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CONTENTS OF VOLUME L.

NUMBER 1.

PAGE

1. **The Trephine in Chronic Glaucoma.** By T. HARRISON BUTLER, Birmingham, England 1

2. **Histology of the Region of the Corneoscleral Margin. Part I. Histology of the Superficial Layer of this Region.** By DR. KAZUO HIWATARI, Kagoshima, Japan. (With four illustrations on Text-Plate I.) 10

3. **Astigmatism—Especially with Regard to the Influence of Age upon the Axis.** By DR. A. W. STIRLING, Atlanta, Ga. . . . 19

4. **Diseases of the Eye Due to Syphilis and Trypanosomiasis among the Negroes of Africa.** By DR. J. N. ROY, Physician to the Hôtel-Dieu, Montreal; Late Special Delegate of the Canadian Government; Laureate of the Academy of Medicine of France . . 28

5. **Sympathetic Ophthalmia. Report of a Case Successfully Treated.** By DR. ALFRED WIENER and DR. ELLIS BONIME, New York 43

6. **Cyclopia, Its Bearing upon Certain Problems of Teratogenesis and of Normal Embryology; with a Description of a Cyclocephalic Monster.** By Dr. EMORY HILL, Richmond, Va. (Concluded.) (With four illustrations in the text.) 52

7. **Perimetric Methods. A Discussion at Oxford Ophthalmological Congress, July, 1920.** By Dr. P. G. DOYNE 81

8. **Report of the Proceedings of the Section on Ophthalmology of the New York Academy of Medicine.** By DR. CONRAD BERENS, JR., Secretary 90

NUMBER 2.

1. **The Ocular Manifestations of Epidemic Encephalitis.** By DR. WARD A. HOLDEN, New York 101

394825

PAGE

2. **On Backing Out of Cataract Operations.** By Dr. H. Gifford, Omaha, Neb. 109

3. **On Methods of Dealing with the Capsule in Cataract Extraction.** By Dr. Arnold Knapp, New York 115

4. **Observation, Management, and Treatment of the Cataract Patient Before and After Operation.** By Dr. Walter H. Snyder, Toledo 120

5. **Metastasis of Carcinoma into an Endothelioma of the Optic Sheath.** By Drs. Martin Cohen and Ward J. MacNeal. (With eleven illustrations on Text-Plates II.–IX.) . . 128

6. **Ocular Manifestations of Disease of the Para-Nasal Sinuses.** By Dr. James Bordley, Jr., Baltimore, Md. (With four illustrations in the text.) 137

7. **Total Keratoplasty.** By Dr. J. W. Burke, Washington, D. C. 147

8. **The Closure of Traumatic Subconjunctival Corneoscleral Fistula.** By Dr. Harry Gradle, Chicago, Ill. With one illustration in the text.) 154

9. **Minor Palpebral and Conjunctival Affections Associated with Refractive and Muscular Errors.** By Dr. John Green, Jr., St. Louis, Missouri 158

10. **Ophthalmology from the Viewpoint of the Clinician.** With three illustrative cases. By Dr. Homer E. Smith, New York. 165

11. **Report of the Transactions of the Ophthalmological Section of the Royal Society of Medicine.** By Mr. H. Dickinson, London 172

12. **Report of the Proceedings of the Section on Ophthalmology of the New York Academy of Medicine.** By Dr. Conrad Berens, Jr., Secretary 176

13. **Correspondence—Foreign Proteids in Treatment of Iridocyclitis.** F. H. Verhoeff 193

14. **Notices** 197

NUMBER 3.

1. **Concerning the Ocular Symptoms in the Subjects of Hypophyseal Disease with Acquired Syphilis; with Illustrative Cases.** By G. E. de Schweinitz, M.D., Philadelphia, Pa. (With five illustrations on Text-Plate X.) 203

2. **The Control of Pituitary Lesions, as Affecting Vision, by the Combined Surgical-X-Ray-Radium Treatment.** By Charles H. Frazier, M.D., D.Sc., Surgeon to the University Hospital, Philadelphia. (With five illustrations on Text-Plates XI.-XII.) 217

PAGE

3. **Molluscum Conjunctivitis.** By Dr. Harold Gifford and Dr. Sanford R. Gifford, Omaha, Neb. (With four illustrations on Text-Plates XIII.-XIV.) 227

4. **Lacrimal Sac Extirpation Simplified.** By Dr. Allen Greenwood, Boston, Mass. (With four illustrations on Text-Plate XV.) 234

5. **Two Unusual Cases of Pterygium.** By Dr. Fumio Yano, in the Eye Department of the "Aichi" Medical College, Nagoya (Japan). (With one illustration in the text.) 239

6. **Bilateral Circumpapillary Chorioretinitis with Detachment of the Retina in Syphilis.** By Dr. Arnold Knapp, New York . 242

7. **Report of a Case of Lipæmia Retinalis with Hypotony in Diabetic Coma.** By Dr. Martin Cohen, New York . . . 247

8. **Report of the Transactions of the Ophthalmological Section of the Royal Society of Medicine.** By Mr. H. Dickinson, London 252

9. **Report of the Proceedings of the Section on Ophthalmology of the New York Academy of Medicine.** By Dr. Conrad Berens, Jr., Secretary 262

10. **Report on the Progress of Ophthalmology.** Abstracts by Drs. A. N. Alling, New Haven; M. J. Schoenberg, New York; T. H. Butler, London; P. J. Doyne, London; and K. Wessely, (*Archiv für Augenheilkunde*), Würzburg. Edited by Matthias Lanckton Foster, M. D., F. A. C. S., New Rochelle, N. Y. . 274

I.—General Ophthalmic Literature, 274; II.—The Eye in its Relations to General Disease, 275; III.—Ocular Diseases, Remedies, and Instruments, 283; IV.—Anatomy, Physiology, Malformations, 289; V.—Refraction, Accommodation, and the Sense of Sight, 293; VI.—The Motor Apparatus of the Eye, 296.

11. **Book Reviews** 299

NUMBER 4.

1. **Phacœrisis.** By Dr. I. Barraquer, Barcelona, Spain. (With thirteen illustrations on Text-Plates XVI.–XX.) 307

2. **Glaucoma and the Nasal (Sphenopalatine (B.N.A.) Meckel's) Ganglion.** By Dr. M. H. Post, Jr., St. Louis, Missouri . . 317

3. **A Mercury Tonometer.** By Dr. Martin Cohen, New York. (With six illustrations on Text-Plates XXI.–XXII.) . . 326

4. **The Surgical Treatment of Epithelioma of the Cornea.** By Dr. L. M. Francis, Buffalo, N. Y. (With five illustrations in the text.) 331

PAGE

5. **The Corneal Suture in Cataract Extraction.** By DR. E. C. ELLETT, Memphis, Tenn. 341

6. **Congenital Atresia of the Puncta Lacrimalia of One Side.** By DR. HARRY GRADLE, Chicago 349

7. **Report of the Proceedings of the Section on Ophthalmology of the New York Academy of Medicine.** By DR. CONRAD BERENS, JR., Secretary 352

8. **Discussion on "Diabetes in Relation to Diseases of the Eye," at the Annual Meeting of the Ophthalmological Society of the United Kingdom, 1920.** By MR. P. G. DOYNE, London, England 378

9 **Report of the Transactions of the Ophthalmological Section of the Royal Society of Medicine.** By MR. H. DICKINSON, London, England 386

10. **Report on the Progress of Ophthalmology.** Abstracts by DRS. A. N. ALLING, New Haven; M. J. SCHOENBERG, New York; T. H. BUTLER, London; P. J. DOYNE, London; and K. WESSELY (*Archiv für Augenheilkunde*), Würzburg. Edited by DR. MATTHIAS LANCKTON FOSTER, New Rochelle, N. Y. 393

VII.—The Lids and Lacrimal Organs, 393; VIII.—The Orbits and Accessory Sinuses, 397; IX.—The Conjunctiva, 399; X.—The Cornea, Sclera, and Anterior Chamber, 404.

NUMBER 5.

1. **The Ophthalmological Findings in Traumatic Asphyxia with the Report of a Case.** By DR. PAUL D. BERRISFORD, St. Paul, Minn. (With one illustration on Text-Plate XXIII.) . 411

2. **Brief Notes on Some Ophthalmological Conditions.** By COL. HENRY SMITH, I.M.S., London, England 422

3. **Report of a Second Hundred Successive Extractions of Cataract in the Capsule after Preliminary Subluxation with the Capsule Forceps.** By DR. ARNOLD KNAPP, New York . . 426

4. **Melanosarcoma of the Choroid Occurring in Brothers.** By DR. ADOLPH O. PFINGST, Louisville, Ky., with Pathological Report by DR. STUART GRAVES, Louisville, Ky. (With three illustrations on Text-Plate XXIV.) 431

5. **Practical Points in Cataract Extraction Emphasized in Col. Henry Smith's Technique for Intracapsular Extraction.** By DR. CLARENCE KING, Cincinnati, O. 440

6. **Treatment after Cataract Operations.** By DR. J. W. MILLETTE, Dayton, O. 446

PAGE

7. **Glioma Retinæ Treated by X-Rays with Apparent Destruction of the Tumor and Preservation of Normal Vision.** By F. H. VERHOEFF, M.D., Boston, Mass. 450

8. **Spontaneous Hypotonus in Juvenile Glaucoma.** By DR. ALFRED H. RIEDEL, New York 457

9. **Report of the Proceedings of the Section on Ophthalmology of the New York Academy of Medicine.** By DR. CONRAD BERENS, JR., Secretary 464

10. **Report of the Annual Congress of the Ophthalmological Society of the United Kingdom.** By MR. H. DICKINSON, London . 471

11. **Report of the Transactions of the Ophthalmological Section of the Royal Society of Medicine.** By MR. H. DICKINSON, London 483

12. **Report on the Progress of Ophthalmology.** Abstracts by DRS. A. N. ALLING, New Haven; M. J. SCHOENBERG, New York; T. H. BUTLER, London; P. J. DOYNE, London; and K. WESSELY (*Archiv für Augenheilkunde*), Würzburg. Edited by MATTHIAS LANCKTON FOSTER, M.D., F.A.C.S., New Rochelle, N. Y. . 486

XI.—The Pupils, 486; XII.—The Uveal Tract and Sympathetic Ophthalmia, 487; XIII.—The Lens, 492; XIV.—Glaucoma and Intraocular Tension, 494; XV.—The Retina and Vitreous, 496; XVI.—Accidents, Injuries, Foreign Bodies, Parasites, 503.

NUMBER 6.

1. **The Treatment of Cataract.** By HENRY SMITH, Colonel I. M. S., London, Eng. 515

2. **Episcleritis—A New Method of Approach.** By DR. H. L. SINSKEY, DR. M. B. LEVIN, and DR. B. SACKS, Baltimore, Md. 526

3. **A Case of Keloid of the Cornea.** By DR. H. D. LAMB, St. Louis, Mo. (With two illustrations on Text-Plate XXV.) . . . 535

4. **Lipæmia Retinalis.** By DR. W. F. HARDY, St. Louis, Mo. . 543

5. **The Physiological Mode of Action of Mydriatics and Miotics—Explaining their Effects in Hypertension (Glaucoma).** By DR. CARL KOLLER, New York 550

6. **The Action of Adrenalin on the Glaucomatous Eye.** By DR. ARNOLD KNAPP, New York 556

7. **The Character of Iritis Caused by Focal Infection.** By WILLIAM L. BENEDICT, M.D., Section on Ophthalmology, Mayo Clinic, Rochester, Minn 560

PAGE

8. **A Case of Intermittent Exophthalmos.** By DR. W. GORDON M. BYERS, Montreal, Canada. (With one illustration on Text-Plate XXVI.) 569

9. **Report on the Progress of Ophthalmology.** Abstracts by DRS. A. N. ALLING, New Haven; M. J. SCHOENBERG, New York; T. H. BUTLER, London; P. G. DOYNE, London; and K. WESSELY (*Archiv für Augenheilkunde*), Würzburg. Edited by MATTHIAS LANCKTON FOSTER, M.D., F.A.C.S., New Rochelle, N. Y. . 574

I.—The Eye and General Diseases and Poisons, 574; II.—Ocular Diseases, Remedies, and Instruments, 578; III.—Anatomy, Bacteriology, Pathology, Malformations, 582; IV.—The Sense of Sight, Refraction, and Accommodation, 586; V.—The Motor Apparatus of the Eye, 591; VI.—The Lids and Lacrimal Apparatus, 592.

10. **Book Reviews** 595

11. **Index of Authors and Subjects, Vol. L.** 603

EDITORIAL NOTICE.

The Archives of Ophthalmology is a bi-monthly journal, published in annual volumes of about six hundred pages each, extensively illustrated with cuts in the text, half-tone text plates, and lithographic plates, many in colors.

About three quarters of the space is devoted to original papers, and the remaining quarter to a systematic report on the progress of ophthalmology, and to reports of societies, book reviews, and miscellaneous notes, all of it original.

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ARCHIVES OF OPHTHALMOLOGY.

THE TREPHINE IN CHRONIC GLAUCOMA.

BY T. HARRISON BUTLER, BIRMINGHAM, ENGLAND.

ONE of the greatest of American writers has expressed the opinion that "a foolish consistency is the hobgoblin of little minds." These words apply with especial force to medical subjects, including the treatment of glaucoma. I do not hesitate therefore to express views which differ materially from those I have published in past years, and which in the light of further experience have proved to be erroneous. In 1915 I contributed a paper to this journal ARCHIVES OF OPHTHALMOLOGY, vol. xliv., No. 6, page 611) in which I cast doubts upon the suitability of sclerotomy as the operation of election in glaucoma simplex. Smarting from the disappointment caused by several serious cases of late infection I too hastily decided to abandon sclerotomy, and in actual fact treated a series of cases of chronic and subacute glaucoma by various forms of iridectomy. The result was disappointing, for careful analysis of all my examples of chronic glaucoma treated by iridectomy showed that but 43% of them were permanently relieved by the procedure. Many of the eyes were subsequently trephined with varying success. I also found that trephining after iridectomy was neither so easy nor so successful as primary trephining. On the other hand all cases of sclerotomy analyzed to the same date yielded a success percentage of 64. It also appeared that Holth's punch operation was more effective in reducing tension than the operation with the 1.5*mm* trephine, but that nearly all the cases of late infection up to

Ed. 12-22-21

this date had followed punch operations. The chief source of failure in these sclerotomies was firm healing of the aperture with cessation of filtration or inadequate filtration. My results at this time formed the subject of a paper which I read to the Midland Ophthalmological Society in 1918 (*Transactions of the Ophthalmological Society of the United Kingdom*, vol. xxxviii., page 368). It had by this time become obvious to me that for some reason difficult to explain the punch operation was more liable to be followed by late infection than the trephine method, and must be abandoned. Also that the 1.5*mm* trephine was too small to yield a sufficient percentage of filtering scars. I therefore began to use a 2*mm* trephine of my own design. The result has been most gratifying. During the years 1918 and 1919 I have trephined over 80 eyes in some 70 patients. Forty-odd of these operations have been undertaken to relieve tension in glaucoma simplex (chronic glaucoma without congestive signs) and, as far as my notes take me, all have been more or less successful. That is to say that at the time the last note was made tension had been normalized or so far reduced that the disease had apparently been arrested. Some of these patients have been observed for over two years, others for not more than a few months. Time will naturally show that a proportion of these eyes are still glaucomatous, in fact the percentage of recovery may easily fall to 80 or 85%; but up to the time of writing, August, 1920, none of these 40 operations has been proved to be a failure. In four more cases the first trephining was unsatisfactory, but subsequent operations were successful. If I combine these operations, 48 in all, with my older trephine operations, 52 in number, we get 100 trephining operations for glaucoma simplex with 23 failures, or a success percentage of 77. Three of the 23 failures were cured by a second or third operation, which gives a final result of 80% successful up to date, and as far as the present history is known. These figures compel me to be inconsistent, and at the present time to hold the view that trephining with a 2*mm* instrument *performed early in the disease* holds out an excellent chance of the long intermission or complete cure of the disease. Let it, however, be understood that these figures apply solely to glaucoma simplex, cases in which the disease is characterized by rise of tension, cupping of

the disk, and contraction of the fields, or enlargement of the blind spot, or both; and that cases with signs of congestion are excluded. The operation in acute glaucoma, subacute glaucoma, and in secondary glaucoma yields other percentages of cure, and the results are far more difficult to analyze because the circumstances vary more than in glaucoma simplex.

During the past two years I have been increasingly impressed with the necessity for early operation. The indications I act upon are raised tension combined with signs of impairment of function. If for example the tension by the Schiotz tonometer is 30, and there are no signs of functional failure or of marked cupping of the disks, I would not operate, but in the presence of such signs I should use a miotic for a few weeks, taking the tension twice a week, and recording it on a chart. If at the end of a month miotics had not reduced the tension I should operate. Were the original tension above 30 I should not wait so long, and above 40 I would not wait at all. Whereas there seems to be a tendency to revert to the use of miotics and to postpone or even omit operation, it would appear that the time is ripe for an exact research upon the action of these drugs in chronic glaucoma. Most of our opinions upon the subject have been handed down from pre-tonometric days and are therefore founded upon an insecure basis. I take it that a miotic lowers tension mechanically by withdrawing the iris from the iridic angle just as atropine mechanically raises tension by the reverse process. If, however, the iridic angle be of adequate patency, as in a normal eye, atropine does not raise the tension, nor does eserine lower it. In some examples of early chronic glaucoma, the anterior chamber is not unduly shallow, nor is the pupil dilated. How then can contracting a normal pupil in a normal chamber lower the tension? My clinical experience is that in such cases a miotic has no such action. On the other hand, in subacute and acute glaucoma with a dilated pupil, if a miotic be successful in contracting the pupil, tension may be lowered, and I have seen more than one case of acute glaucoma in which the free use of eserine and morphine has lowered the tension, reduced the congestion, and greatly facilitated iridectomy. Again there are late cases of chronic glaucoma with a narrow iridic angle

and a dilated pupil in which the tension falls if the pupil can be got to contract.

Careful observations with the tonometer in cases with normal chamber and pupil should decide the question finally. I personally am doubtful as to the permanent efficiency of miotics in eyes without shallow chambers, and I wonder whether some at least of the cases which are said to do well on miotics would not do equally well without any local treatment. General attention to the health is I think more important. I prefer to reserve miotic treatment for cases in which, owing to age, to nervous instability, or to other circumstances, operation is contraindicated. I have not yet satisfied myself that miotics have any permanent value in glaucoma simplex, and *if their use tends to postpone operation much harm is done.* I am fully aware that these opinions are heterodox and I am prepared to change them at once when I obtain proof of the value of local drug treatment.

Some surgeons believe that when the contraction of the field menaces the fixation point any operation is apt to cause total loss of central vision and that iridectomy is especially dangerous. In my own practice this has happened but twice, once after iridectomy, once after sclerotomy. My own view is that *the more the fixation point is menaced either by contraction of the peripheral field or by the presence of a Bjerrum scotoma the more urgent is immediate operation.* I have trephined several such cases with and without iridectomy. All have been successful except one. When the field of vision is contracted to within a few degrees of the fixation point, blindness if the case is left alone is a matter of months or even weeks, whereas operation offers a splendid prospect that the rapid contraction will cease, and in one or two cases I have seen a large increase in the fields of vision. In a few exceptional cases contraction of the peripheral fields and the formation of scotomata has continued although the tension has been normalized by operation.

The operations recorded have been performed upon my private patients, at the Birmingham Eye Hospital, and in the Ophthalmic Clinic attached to the General Hospitals at Coventry and at Leamington Spa.

In nearly all the patients operated upon in 1918 and in 1919 the tension has been recorded by the Schiotz tonometer, and

in many cases it has been charted upon my tonometric chart.

The peripheral fields have been carefully studied, and when necessary the central area has been explored with the Bjerrum screen, now I believe called the tangent screen. In hospital practice there is little time for work of this nature, but a rapid test has been made in all cases of doubt to exclude or confirm the presence of a central scotoma. In more than one patient the presence of a Bjerrum scotoma has been the sole change detected in the field.

The operations have been carried out according to the most recent Elliot technique. Cocaine in 4% solution is instilled three times; the first instillation being combined with one of a 1.0% solution of eserine to avoid dilatation of the pupil. The conjunctiva is seized with straight iris forceps and reflected to the limbus with squint scissors. The conjunctiva is now further reflected with a few strokes of a Landolt scalpel till the gray crescent appears in the cornea. I find that if the scalpel be applied to the exact spot where the conjunctiva leaves the cornea little progress is made, if, however, it be applied slightly forward onto the conjunctiva itself, say about half a millimeter away from the corneal aspect, the progress is easy. Great care is taken to make the flap as thick as possible. The *2mm* trephine is applied as close to the line of reflection as possible, and tilted to cut the sclera in trapdoor fashion. The disk is now seized together with any prolapsed iris and excised. If the iris does not prolapse I do not fish for it and omit the iridectomy. The flap is sewn in place by a single suture. The dressing is removed next day and atropine instilled. This is repeated daily if any undue injection be noted. Few of the operations occupied more than ten minutes, the majority about five or six minutes. The only real drawback that has appeared in the last series of cases is the occasional formation of a large ectatic bleb. These patients have so far done well and appear to be more permanently benefited than those with a more beautiful type of scar. In a few cases the anterior chamber has remained shallow for a fortnight. There seems to be a tendency for a nuclear cataract to develop, and some of the older operations which were originally classed as successful should for this reason be reclassified as partial failures. This is one of the com-

plications which will tend to reduce the percentage of success in the series under review from 100 to 80 or thereabouts. Iritis was occasionally noticed but gave no trouble.

Late infection. In addition to the examples of this complication which I published in the *Ophthalmoscope*, vol. xiii., p. 370, I have a few more to recount—two of them in patients who have already had previous attacks, and two primary cases. These I hope to record in another paper. Their presence shows that late infection is indeed the tragedy of sclerotomy, but in view of the high percentage of success obtained from the operation and its marked superiority in other respects, we can only regard them as part of the toll glaucoma demands.

The results in absolute glaucoma even when there are no congestive signs are not very satisfactory; in the presence of congestion they are very poor. It is probably wiser to remove painful eyes when inflamed, for trephining offers but a slender chance of relief. In non-congestive but painful absolute glaucoma I leave the choice of operation to the patient.

OPERATIONS FOR GLAUCOMA SIMPLEX 1918 AND 1919

Name	*T. before operation*	*T. after operation*	*V. before operation*	*V. after operation*	*Nature of operation*	*Remarks*
1 Duckett	45	19	6/18	6/18	T c I	Seen 10 months after operation.
2 "	55	32	6/18	6/12	T c I	Fields before operation all within 5° circle. No change after operation.
3 Plummer	38	14	6/9	6/9	T c I	Deep cups and very small fields, concentric contraction.
4 "	60	17	H. R.	6/60	T c I	Fields smaller when last seen.
5 Perry	85	− 2	1/60	3/60	T c I	Deep cup and shallow anterior chamber.
6 Bowbotham	60	Tn	6/6	6/5	T c I	Ideal filtering scars.
7 "	80	Tn	6/6	6/5	T c I	
8 Jones	35	10	6/60	6/18	T c I	Nasal step in field. Good increase in acuity.
9 Stevens	45	23	6/9	6/9	T	Had a Herbert's wedge isolation done a year before this operation.
10 "	34	30	< 6/60	< 6/60	T	A fair result only. A very late case.
11 Wells	33	13	6/12	6/12	T	The other eye had an iridectomy 20 years ago for acute glaucoma. T. 15.
12 Blyth	50	10	6/18	6/12	T	Large ectatic scar. Nasal half of field gone. Seen 2 years later. Result still good.
13 Tiffany	48	32	< 6/60	< 6/60	T	Almost absolute glaucoma. A year later no pain, disk not cupped.
14 Law	35	Tn	6/6	6/6	T	Fields increased after operation.
15 "	35	Tn	6/60	6/36	T	Disks became less cupped.
16 Butler	47	17	6/24	6/24	T c I	
17 Ray	40	29	6/60	6/60	T	Minute central field only 1–2 degrees. There is an isolated seeing island on temporal side.
18 Bassett	80	34	6/18 −	6/18 −	T c I	Iridectomy in 1915 did not reduce T.
19 Brewer	60	− 1	Fingers	Fingers	T c I	Seen some months later. Fields and vision well maintained.

OPERATIONS FOR GLAUCOMA SIMPLEX 1918 AND 1919

	Name	*T. before operation*	*T. after operation*	*V. before operation*	*V. after operation*	*Nature of operation*	*Remarks*
20	Spencer	60	8	$^6/_{18}$	$^6/_{18}$	T c I	3 months later good vision and satisfactory eyes in spite of hypotony.
21	"	44	8	$^6/_{12}$	$^6/_{12}$	T c I	Before operation rapid loss of fields.
22	Smith	100	12	< $^6/_{60}$	$^6/_{36}$	T c I	Note the increase in acuity.
23	"	60	22	$^6/_{60}$	$^6/_{36}$	T c I	
24	Lewis	66	18	Fingers at 2m	$^6/_{12}$	T c I	Great increase in acuity. Scleral puncture before trephine.
25	"	60	29	"	$^6/_{60}$	T c I	
26	Jakeman	68	20	$^6/_{36}$	$^6/_{12}$	T	Late infection, 7 months after operation.
27	"	68	20	P. L.	No P. L.	T	
28	Clarke	62	25	$^6/_{12}$	$^6/_{18}$	T c I	Very small fields became almost normal.
29	"	62	25	$^6/_{18}$	$^6/_{36}$	T c I	Lens remained forward 14 days. Slight iritis and synechiæ.
30	Showell	55	17	Fingers	$^6/_{24}$	T	Note increase in acuity.
31	"	50	8	"	$^6/_{18}$	T c I	
32	Clews	60	14	P. L.	P. L.	T c I	
33	Crooks	?	26	$^6/_{12}$	$^6/_{12}$	T	Original notes mislaid.
34	"	?	18	$^6/_6$	$^6/_6$	T	Trephined for raised tension.
35	Dalton	60	5	$^6/_{35}$	$^6/_{18}$	T c scleral puncture	
36	Harrison	63	20	$^6/_{36}$	$^6/_{12}$	T c I	
37	Filby	70	27	$^6/_8$	$^6/_{12}$	T c I	Left eye had had an iridectomy. T. still 45.
38	Gluther	60	− 2	< $^6/_{60}$	< $^6/_{60}$	T	Cataract. Second operation, had late infection after first.
39	Belfield	70	25	$^6/_{60}$	$^6/_{60}$	T	Has had four trephines, last one produced an ectatic scar, and was successful.

OPERATIONS FOR GLAUCOMA SIMPLEX 1918 AND 1919

Name	*T. before operation*	*T. after operation*	*V. before operation*	*V. after operation*	*Nature of operation*	*Remarks*
40 Gray	45	10	6/60	6/60	T	4th trephine produced an ectatic scar and reduced T. Had a slight late infection a month after operation.
41 Beasley	70	19	P.L.	P.L.		First hole closed up, operation repeated.
42 "	61	22	"	"		
43 Rice	50	7·5	6/6	6/6		
OPERATIONS FOR ABSOLUTE GLAUCOMA						
Dalton	60	8	No P.L.		T	Trephined to relieve pain with success.
White	48		"		T	Eye became injected and was excised. A very late case.
Edinburgh	44		"		T	No relief of pain or tension.
Brewer	140	140	"		T	Pain relieved but eye still stone hard. Fibrous mass on site of operation blocked hole.
Salt	60		"		T	No result. Hole blocked with iris tissue.
Priest	72	?	"		T	Died at home, final result unknown.

HISTOLOGY OF THE REGION OF THE CORNEO-SCLERAL MARGIN.

PART I. HISTOLOGY OF THE SUPERFICIAL LAYER OF THIS REGION.

BY DR. KAZUO HIWATARI, KAGOSHIMA, JAPAN.

(With four illustrations on Text-Plate I.)

THERE is many a hiatus in our knowledge of the histology of the corneoscleral margin, and some of the known conditions have admitted of various interpretations. For instance, no mention is made anywhere of the rare congenital condition, which I am the first to describe, of an island of mucous membrane in this region covered with cylindrical instead of flat epithelium, and, as will be shown later, Manz (2), Ciaccio (3), and H. Virchow (1) differ in their descriptions of the ridgelike formation of the subepithelial layer of the limbus. A consideration of these facts has led me to regard this region as a field for new, accurate histological work.

MATERIALS AND METHODS.

It is evidently very desirable that such an investigation as this should be prosecuted with material fixed while warm with life, but this is difficult to accomplish. I collected the material in the winter, usually from four to forty-eight hours after death, and fixed it either in a 10% solution of formol, or in Orth's mixture. In removing the eyeballs the globes were extirpated together with the lids, so that the bulbar conjunctiva should be spared as much as possible. After fixation was sufficient the

region of the limbus was carefully dissected off. The sexes and ages of the individual cases were as follows:

Case	*Sex*	*Age*
1	m.	40 days
2	f.	60 days
3	m.	10 months
4	m.	13 years
5	m.	17 years
6	m.	20 years
7	m.	24 years
8	m.	28 years
9	f.	29 years
10	m.	45 years
11	m.	58 years
12	m.	68 years
13	m.	79 years
14	f.	80 years

The celloidin method was used for the preparation of the sections, which were cut sagittally, horizontally, and parallel to the surface (surface sections), part of them in series, varying for the most part from 8 to 14 μ in thickness. The stains used were hæmatoxylin (Boehmer)-eosin, Weigert's hæmatoxylin and van Gieson, Unna-Pappenheim's methyl green pironin, and the elastic stain (Weigert's method and orcein). For comparison I used many microscopic preparations in the collection belonging to this ophthalmological clinic. Furthermore I used Kiyono's lithioncarmine vital stain on some rabbits' eyes in order to ascertain as accurately as possible the kinds of cells in the subepithelial layer of the limbus.

HISTOLOGICAL FINDINGS.

It is necessary first to define the margins of the limbus, as these have been fixed differently by different authors. I agree with H. Virchow (*l. c.*) in considering the limbus to be the segment of conjunctiva which begins toward the cornea at the end of Bowman's membrane and extends toward the fornix to a place overlying Schlemm's canal. The breadth of the limbus corneæ so defined, the conjunctiva cornealis of H. Virchow, is about 2μ according to that writer. But as this breadth is clinically demonstrable to vary in different places, I measured

it in four different directions and present the results in the following table:

Age	*Sex*	*Breadth of Limbus*			
		Above	*Below*	*Nasally*	*Temporally*
40 days	m.	1.20μ	0.80μ	0.80μ	0.80μ
60 days	f.	1.20	1.00	0.80	0.80
10 months	m.	1.40	1.20	1.00	1.00
13 years	m.	2.25	1.50	1.20	0.95
17 years	m.	2.00	1.80	1.00	1.00
20 years	m.	2.25	1.95	1.50	1.50
24 years	m.	2.00	1.50	1.00	1.00
28 years	m.	2.25	1.80	1.20	1.20
29 years	f.	2.00	1.95	1.20	1.20
45 years	m.	2.00	1.50	1.00	1.00
58 years	m.	1.80	1.50	1.00	1.00
68 years	m.	2.00	1.50	1.20	1.20
79 years	m.	2.00	1.80	1.50	1.50
80 years	f.	2.25	1.80	1.50	1.50

As one can see from this table the breadth is regularly greatest above, somewhat less below, and still less, but about equal, nasally and temporally.

A. THE EPITHELIAL LAYER.

The construction of the epithelial layer was described first by Manz (*l. c.*), but most accurately by H. Virchow (*l. c.*). According to the latter the epithelial layer is composed of six layers at a distance of about 60 cylindrical cells breadth from the end of Bowman's membrane, and presents rather the type of the corneal epithelium, while laterally it comes to resemble more and more the conjunctival, in that the cylindrical basal cells change into cuboidal and the superficial flat cells gradually become larger. From six to thirteen layers are to be found between the elevations of the tunica propria, which will be discussed later.

One needs to be very careful in counting the number of layers of epithelium in cadaveric material, as the epithelial layer is very easily broken down, and the epithelia thrown off, by the post-mortem maceration. The material must therefore be as

fresh as possible. My eighth case, a man 28 years old who died from ileus, but was otherwise sound, was best suited for this purpose. Six hours after death the eyes were extirpated with the observance of every precaution and prepared. I counted the number of layers in this material and found, in agreement with Virchow, that they were from ten to thirteen over the depressions and from five to seven over the elevations. The deepest layer of epithelium was cylindrical, the middle polygonal, and the superficial flat.

The pigmentation of the limbus epithelium, which, according to Kopsch (13), was demonstrable in one third of all Europeans examined, was observed also by Virchow (*l. c.*). According to the latter it is most marked in the basal cells and gradually decreases toward the surface. The pigment appears in the form of red brown, roundish granules in the cell body, closely grouped on the distal side of the nucleus portion.

I have found this pigmentation to be quite constant, whence it may be concluded that this condition is regularly present in the colored races. The degree of pigmentation varies in different cases, and in different places in the same case. When it was very marked the pigment was abundant in almost all the epithelia, but much more so in the deeper than in the superficial layers. Such marked pigmentation was present in cases 7, 10, 11, 12, and 13. Slight pigmentation, in which only the epithelia in the deeper layers were affected while those in the superficial were for the most part free from pigment, was shown in cases 1, 2, and 3. The remaining cases, 4, 5, 6, 8, 9, and 14, were moderately pigmented, in that pigmented epithelia were present only in the basal and middle layers of cells. Although the number of children is not large enough to warrant any deductions, the conclusion that in general the pigmentation is less in children than in adults seems to me to be justified, because I found it to be less in them than in the least pigmented cases in adults. The pigmentation was so sparse in the children that it could be demonstrated only under a high magnifying power.

The varying degree of pigmentation in different places in the same case was striking. Questioning whether this might not be due to the effect of light, I determined the pigment content of the upper part of the limbus, which had been covered during

life by the upper lid, and of the portion in the palpebral fissure, which had not been protected from the light, and compared the two in five cases. Contrary to my expectations the former proved in each case to be the richer in pigment. This proves incorrect the suggestion of Fischer (12), that the pigmentation of the limbus may possibly be to protect the eye from too much light.

I wish to mention here two original observations made by me in regard to the pigmentation: the occurrence of pigment in the epithelium of the cornea adjoining the limbus, and of chromatophores in the subepithelial layer. The former was met with in only five strongly pigmented cases, and the number of the pigmented epithelia was small. In the very strongly pigmented Case 12 I counted seven pigmented epithelia in one section (Fig. 1), while in the other cases I could find only two or three. In Fig. 1 we see that the pigmented epithelia extend to a place about ten basal cells breadth beyond the end of Bowman's membrane, and that they are both basal and superficial.

Chromatophores were found in all cases. The number varied, but in general was greater the more strongly the subjacent layer of epithelium was pigmented. Yet the number was not great, even in the most strongly pigmented Case 12, for they did not occur in every section. Neither of these two conditions has hitherto been described by anyone, although the eyes of the colored races have often been used for examination—Giacomini (11), Steiner (10), Fischer (*l. c.*).

H. Virchow (*l. c.*) says that mucous cells, which he denominates wandering mucous cells, are very rarely to be met with in the conjunctiva cornealis. I found them only in a single case, that of a boy 13 years old (Case 4). I found them in the upper part of the limbus, quite superficial and typically globular, surrounded by flat epithelium with no cylindrical epithelium to be found in their neighborhood. The total number in four series of sections 12μ thick was thirteen. When they occur at all in the limbus they are confined to a very small area, never close together, but always with a variable number of ordinary epithelia between two neighboring mucous cells. Whether this is always the case or not must be determined by future researches.

Wandering cells occur singly in this region, especially in the

EXPLANATION OF FIGURES ON PLATE I.

FIG. 1. Marked pigmentation of the epithelial layer of the limbus. Not only the epithelium of the limbus, but also of the cornea to Bowman's membrane is pigmented. The number of the pigmented epithelia in the latter is 7. Zeiss DD, Komp. Ok. 6.

FIG. 2. A surface section of the limbus. The netlike arrangement of the elevations of the tunica propria are here unmistakable. Leitz 3, Ok. 3.

FIG. 3. A section from the limbus of a vital stained rabbit's eye. The cells with granules are Kiyono's histiocytes. The granules are black instead of red. Zeiss DD, Komp. Ok. 4.

FIG. 4. Marked pigmentation of the epithelial layer of the limbus; almost all the epithelia are laden with pigment. Chromatophores are to be seen in the subepithelial layer. Zeiss DD, Komp. Ok. 6.

ILLUSTRATING DR. KAZUO HIWATARI'S ARTICLE ON "HISTOLOGY OF THE REGION OF THE CORNEOSCLERAL MARGIN."

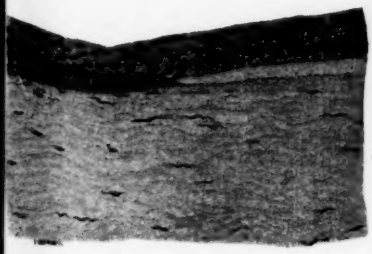

FIG. 1.

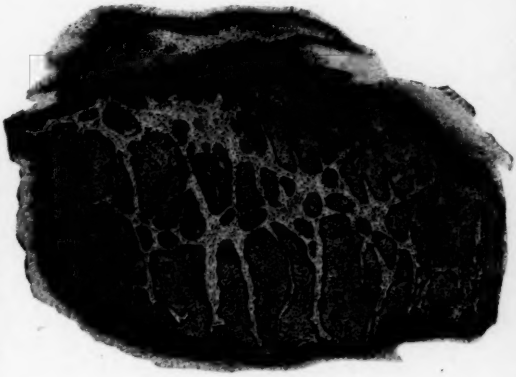

FIG. 2.

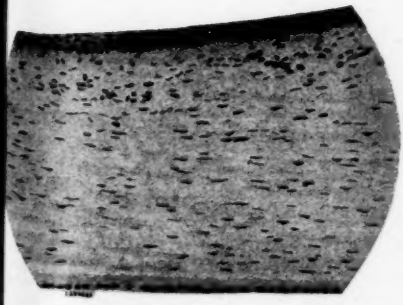

FIG. 3.

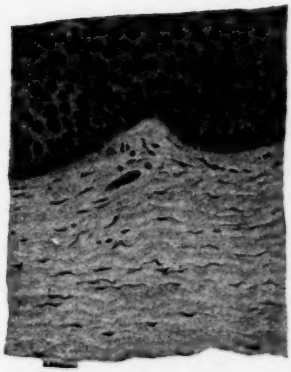

FIG. 4.

basal layer, where they are more abundant than in the cornea, but I have never seen such a dense infiltration with them as was described by H. Virchow.

An interesting condition, to which I have already called attention in a former work (9), is the occurrence of an island of mucous membrane which, presenting the character of the fornix, is covered with laminated cylindrical cells. I was able to find this in only three out of 120 preparations belonging to this clinic, that is, in about 2.50 per cent. In my former paper I expressed my opinion concerning the signification of this anomaly in the pathology of the conjunctiva.

B. TUNICA PROPRIA

The tunica propria of the region of the limbus consists of a loose connective tissue continuous with the subconjunctiva and episcleral layers, which blend together in denser fasciculi to pass over finally into the corneal tissue. Elastic fibers which approach the end of Bowman's membrane are mixed with this connective tissue. The tunica propria is quite vascular because of the marginal loops and network of vessels. At the margin of Bowman's membrane, where the connective tissue fibers are dense and scarcely to be distinguished from the corneal tissue the lumina of the loop forming capillaries may be seen close beneath the epithelium. No differences of opinion now exist concerning any of these conditions.

There is not the same unanimity of opinion with regard to the nature of the papillary elevations to be met with here. The first writer to mention the presence of these elevations at the limbus was Manz (*l. c.*), who described them as a narrow ridge in which the elevations were joined together like a network. This was confirmed later by Ciaccio (*l. c.*). Both of these writers found them above and below, but on neither the nasal nor the temporal sides. Arnold (4) and Henle (5) disagreed with Manz and thought these ridges to be artificial folds of mucous membrane, but this idea was soon negatived through the point made by Ciaccio (*l. c.*) that if such were the case the epithelium would have to take part in the formation of the elevations. Nakagawa (6), who included various kinds of mammals in his researches, demonstrated the presence of these

elevations in different animals, but found them to be most marked in man. He believed them to be papillæ, as did also Salzmann (8) and Stoehr (7). H. Virchow (*l. c.*) studied the ridge formation of the propria in a surface preparation according to Semper's dry method, and declared the condition to be not one of a network, as Manz and Ciaccio thought, but one of very fine, closely adjoining, sharply defined little crests arranged in a radiating manner. They were present everywhere except in a small segment on the nasal and temporal sides, and their greatest breadth was 0.5μ.

My own observations compel me to take a position in opposition to Nakagawa, Salzmann, and Stoehr, and to deny that the elevations partake of the nature of papillæ. They look like true papillæ when seen in meridional sections, but one can easily convince himself by examining surface sections that they are not papillæ, that they are ridge formations. It is scarcely possible for a doubt to exist after an examination of Fig. 2. The error made by the above-named authors may perhaps be due to the fact that they studied meridional sections only. Nakagawa certainly did not study surface sections; Salzmann and Stoehr made no positive statements in this regard. In respect to the conflicting statements of Manz and Ciaccio on the one hand and H. Virchow on the other, concerning the arrangement of the little crests, I have to agree with the former as I always found the netlike arrangement in my surface sections (Fig. 2). It is hard to understand how such a difference of opinion could arise between two such men as Manz and H. Virchow. It may be that the trouble lay in the different methods employed in the examination. In the so-called dry method of Semper, used by H. Virchow, the surface of the mucous membrane is denuded of epithelium by maceration and is then studied with a loupe, and it is hardly necessary to point out how inferior in exactitude such a method is to the microscopical examination of surface sections, particularly when the latter are made in series. These ridgelike formations seem to be absent in infants, as I was totally unable to find them in a 40 days old child (Case 1), and found them only above in a 60 days old child (Case 2). The breadth of the zone at its broadest place was 1.35μ, according to my measurement. Most of the elevations, not

all, as Nakagawa states, contain capillary vessels like true papillæ.

No positive statements have hitherto been made concerning the nature of the cells in the tunica propria of the limbus. Nakagawa (*l. c.*) simply mentions the presence of round cells there without discussing their nature. In my opinion these round cells are not all alike, but consist of scattered lymphocytes, plasma cells, and histiocytes of Kiyono (klasmacytes of Ranvier), the last of which may be shown most clearly in sections from the vital stained rabbit's eye (Fig. 3). The presence of chromatophores in the tunica propria I have mentioned already in the description of the pigmentation of the epithelium. For the most part they are spindle-shaped and lie mainly in the upper third of the subepithelial layer, though sometimes deeper, and chiefly in the neighborhood of the capillaries. The nucleus is pale, spindle-shaped, and usually provided with two or three nuclear corpuscles. The granules of pigment contained in them are quite like those in the epithelia (Fig. 4).

RÉSUMÉ.

1. The pigmentation of the epithelium of the limbus corneæ (conjunctiva cornealis) is constant among the Japanese, but varies in degree, while, according to Kopsch, it was present in only a third of the Europeans examined. Generally speaking the pigmentation is less in children than in adults. In each case the portion covered by the eyelid is more pigmented than that in the region of the palpebral fissure.

2. The pigmentation of the epithelium sometimes extends into the cornea adjacent to the limbus.

3. Chromatophores are a constant finding in the propria.

4. The last two findings are quite new and are described for the first time by me.

5. Two variations in the epithelium of the limbus were noted—an island of mucous membrane with cylindrical epithelium, and a circumscribed portion of mucous membrane with beaker cells. The former was found in 2.5 per cent. of 120 cases examined, the latter in a single case out of fourteen.

6. The tunica propria of the limbus presents elevations in

the form of ridges, not of papillæ, which are most distinct above and are wanting on the nasal and temporal sides.

7. The ridges have a netlike arrangement as described by Manz. The degree of their development varies in different cases; they were completely absent in an infant 40 days old.

8. Four kinds of cells may be distinguished in the tunica propria of the limbus—lymphocytes, plasma cells, histiocytes, and chromatophores.

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ASTIGMATISM—ESPECIALLY WITH REGARD TO THE INFLUENCE OF AGE UPON THE AXIS.

By Dr. A. W. STIRLING, Atlanta, Ga.

I BELIEVE that one is correct in saying that the common understanding among ophthalmologists in relation to the axis of the correcting convex lens in astigmatism still continues to be that it tends to be vertical, and of the concave lens that it tends to be horizontal. Indeed ophthalmologists are accustomed to speak of such astigmatism as being "According to the Rule," while the opposite tendency is one "Against the Rule." The position of the axis also is supposed to remain generally more or less permanent. But the figures set out in the following paper appear convincingly to demonstrate that this is such a partial truth as to be in reality no truth at all. They show rather that the axis tends to rotate with age, until in the later decades of life the "Rule," inclines to be entirely reversed. In the spring of this year I wrote an article upon this subject[1] from which I shall here take the liberty of quoting:—"For some years an impression has been growing upon the writer that there exists a definite relationship between age and the axis of astigmatism. This impression, which gradually grew into a conviction, was that the 'Rule' which says that the axis in hypermetropic astigmatism tends to be vertical, while correct for young people is the reverse of correct for the elderly, and that therefore in middle age the axis takes a middle course. How completely the conviction is supported by the facts will appear in this paper. It is possible that this question has already arisen and been examined and settled, but if so the fact

[1] *British Journal of Ophthalmology*, vol. iv., no. 11.

has escaped the writer, while a friend who was recently resident for three years in the New York Eye and Ear Infirmary, in which certain of the surgeons pay much attention to refraction, states that the conclusions which follow are entirely new to him. About the year 1894 the writer on a number of occasions watched his friend, the late Dr. George Bull, in his consulting rooms in Paris at work on refraction cases in which he took much interest. He was greatly occupied with the various causes of blurred vision, among them of course astigmatism; and I remember that he laid particular stress upon the 'clignement,'[1] of the lids in producing at least temporary astigmatism, which would naturally be 'According to the Rule.' He afterwards published two or three papers on this subject[1] which I believe were well received by ophthalmologists. For instance, Parsons says[2]: 'Perhaps the pressure of the lids on the globe tends to squeeze it above and below.' . . . To test the question the writer considered that the fairest method would be to take old cases as they came in his card system, using no diseased eyes, and record them in tabular form. He began strictly according to that rule, but later modified it to this extent: he decided that one is more liable to error with the small degrees of astigmatism, and after having recorded a number of eyes with .25 D. and .37 D. he passed cases of these amounts and noted only .50 D. and over. Later as his time was limited he decided to pass all ages between 20 and 50 of which he had already included a considerable number, and rather to stress the contrast between the astigmatism of the eyes under 20 and that of those over 50 years old. Except for these particulars cases were recorded as they came in the cards."

It has since appeared to the writer that the subject was worthy of more effort, and he decided to continue the investigation upon a larger scale. The present article is the result, and in it are incorporated the eyes used in the other, a summary of whose figures, however, for the sake of comparison, is also set down. It was decided to begin in the case records where the

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[1] "Lid Pressure on the Cornea," *Trans. Intern. Ophth. Congress.* Edinburgh, 1894, p. 107; and "Visual Effects of Refractive Error," *Trans. Ophth. Soc. of U. K.*, 1896, vol. xvi., p. 200.

[2] *Diseases of the Eye*, p. 52.

previous article had left off, to take as I had done before each as it came, and to put down whatever therein appeared relative to the investigation in all the cards contained in a certain number of drawers. I mean by this to make it clear that there was no choice of records, but that the figures which occur are the result of the mere chance of the alphabetical arrangement of the card system. The following restrictions were, however, observed. I have quoted those used in the other paper which referred to the first 200 eyes as they appeared on the records. The restrictions were similar for the eyes that followed, modified to this extent:—in hypermetropic cases it was not considered necessary farther to demonstrate that in young people the axis tends to be vertical, "According to the Rule," and therefore no eye was recorded under 50 years old. But as there had been an insufficient number, only 23, of myopic eyes examined in the former article it was desirable to bring out the contrast, if there were any, between the first two and the later decades of life, and therefore in the second series to record the myopic eyes of patients in the first two and in those decades after 50 years of age. It may be stated that in practically all eyes under 40 years old a cycloplegic (2 per cent. homatropine and cocaine) was used, and that none was used in the majority of the other eyes. No diseased eye was included; and when only one of a patient's eyes was astigmatic it was not used. The eyes of coloured people were excluded.

As in the previous article the method pursued in the investigation "was to mark on a table of ruled paper the number of the case, the age in decades, the amount and kind of the astigmatism, and the axis. The exact degree of the axis was not recorded, but the test frame was divided into sections of 15 degrees each, while the vertical axis (90 degrees) and the horizontal axis (180 degrees) had each a separate column. It was simpler to use a test frame in which the figures beginning on each side at the nose increased downwards to 90 and then upwards on the temporal side to 180, like the old English frame, and similar to the American in the left eye but differing on the right. The following is an example, and shows the first three lines of a table, the x of course indicating to which section the axis belonged.

Should someone else wish to make similar investigations and

R. E. with cyclo.	No. of Case	Age in Decades	Degrees														Ast. in D	
			90	90 to 75	90 to 105	75 to 60	105 to 120	60 to 45	120 to 135	45 to 30	135 to 150	30 to 15	150 to 165	15 to 0	165 to 180	180	+	−
	I.	2	x														.50	
	II.	7									x						1.0	
	III.	2														x		.75

care to follow this method I would suggest that a slightly greater degree of accuracy might be attained by avoiding the repetition of the same degrees. It may be observed that I have for instance 90 to 105, and also 105 to 120. When the axis is 105 it might be registered in either column. I stupidly failed to notice this until I had done some work upon this paper, presumably because I had always used the column to the left. In the present paper the right was therefore preferred, and if we compare the results we find that the effect of the oversight was negligible. To give the tables in full would occupy great space. A mere summary of the results will suffice.

The total number of eyes registered was 544, of which 416 were hypermetropic, and 128 myopic. Of the hypermetropic eyes 107 were under 50 years of age, 309 over 50; of the myopic 79 were under 50, 49 over 50. (The odd figures are accounted for by the fact that in a few cases one eye in the same person was hypermetropic, the other myopic.) Myopia is not common in the Southern States.

As has been already said, after a few of the lower denominations of astigmatism (19 of plus .25 D. and 4 of plus .37 D. but none which was myopic) had been included it was decided to use only those of .50 D. and upwards, because axial error is thus less likely.

The average degree of hypermetropia registered was .87 D. (In the previous article the figures were .83 D.); of myopia 1.02 D.; of the two combined .91 D.

The averages were worked out for each decade separately, and do not appear to have any definite variation with age, but run for hypermetropia in no distinct order from .50 D. to 1.35 D., and for myopia from 1.0 D. to 2.0 D.

The point of main interest in these observations lies in the apparent rotation of the axis with advancing years, and this seems to apply to myopia as well as to hypermetropia (a vertical plus lens of course corresponding to a horizontal minus lens), and as will immediately appear this seems to be a very usual occurrence. Thus, of 107 hypermetropic eyes under 50 years old 17 or 15.9 per cent. were more nearly horizontal than vertical; of 309 hypermetropic eyes over 50 years old 196 or 63.4 per cent. were more nearly horizontal. (In the previous article these figures were respectively 15 and 75.)

Of the 79 myopic eyes under 50 years old 54 or 68.3 per cent. were more nearly horizontal than vertical; and of the 49 myopic eyes over 50 years old 18 or 36.7 per cent. were more nearly horizontal than vertical.

Taking the decades separately from the first to the ninth in the hypermetropic eyes those nearer horizontal than vertical were in percentages: Decade I, only 2 eyes, O; II, 38 eyes, 10.5; III, 26 eyes, 11.6; IV, 26 eyes, 23.1; V, 15 eyes, 27.0; VI, 163 eyes, 55.9; VII, 111 eyes, 70.2; VIII, 33 eyes, 76.6; IX, 2 eyes, 100. In the previous paper the percentages for hypermetropic eyes, missing out decades I and IX in each of which there were only 2 eyes (vertical in the first, horizontal in the ninth), were respectively from the second to the eighth: 10.6; 15.4; 23.0; 27.0; 56.3; 60.0; 83.3; a series of figures showing a like gradation, and very similar steps.

In the myopic eyes the percentages of those more nearly horizontal than vertical were: Decade I, 4 eyes, 100; II, 62 eyes, 69.3; III, IV, V, combined, 13 eyes, 53.8; VI, 35 eyes, 40; VII, 13 eyes, 37.7; VIII, 1 eye, 0; IX, no cases.

In this as in the previous article the average distance of the axis from the horizontal in each decade was measured by using the middle figure of each of the above-mentioned segments of 15 degrees each, which is close enough for our purpose. These distances were in the hypertrophic eyes from the first to the ninth decades respectively in degrees 83.0; 75.4; 75.8; 65.6; 59.5; 38.5; 29.9; 23.7; and 4.0.

The myopic eyes gave the following distances of the axes from the horizontal: for the first two decades combined (there were only 4 eyes in the first decade) 25.7; for the third, fourth, and fifth decades combined 46.7; for the sixth 51.6; and for the seventh 55.3.

It seems fair to conclude from the above series of figures that we must modify the so-called "Rule" for astigmatism, which appears to be true enough for young eyes, but the reverse for the elderly; and also that there is quite commonly a rotary movement of the axis proceeding slowly with the passage of time.

In the previous paper it was stated that the rotation did not appear to occur much more commonly in one direction than the other, because in hypermetropic oblique astigmatism the axis

was found in the eyes under investigation to run down and out in 57 per cent. and down and in in 43 per cent. In the hypermetropic eyes with oblique astigmatism of the present article (47.5 per cent. of all the hypermetropic eyes) the axis of the correcting convex lens ran down and out in 59.6 per cent. and down and in in 40.4 per cent. In the myopic eyes with oblique astigmatism (54.7 per cent. of all the myopic astigmatic eyes) the axis of the correcting concave lens ran down and out in 32.8 per cent., and down and in in 67.2 per cent.

There does, therefore, appear to be in both hypermetropic and myopic eyes distinctly greater tendency for the meridian of greater corneal curvature to wheel towards the nose than away from it; that is, presuming the astigmatism to be corneal, a question which might best be settled from the records of those who use an ophthalmometer.

Another method of investigating the question of this axial rotation would be through the histories of the same eyes during long periods. Of course comparatively few such cases are available. In going over my notes, however, I have come across a number of which the following is the most illustrative because the most fully recorded case. The patient's astigmatism between 1905, when he was 47 years old, and 1918, the year of the last examination, showed a tendency to vary from plus .50 D. to plus .37 D. or plus .25 D. The right axis in 1905 was 75 degrees from the horizontal; in 1906, 1907, and 1908 it was practically the same; in 1915 it was only 45 degrees, and in 1916 20 degrees from the horizontal. The left eye in 1905 was 65 degrees; in 1906, 1907, and 1908, 55 degrees; in 1915, 45 degrees; in 1916, 15 degrees from the horizontal; and in 1918 it was horizontal.

But I have also noticed a couple of hypermetropic cases in which after an interval of years the axis had swung away from the horizontal. It is quite possible that further observation may show that it occasionally happens that axes beginning at 180 degrees turn away from the horizontal. Why they should so begin, and why they should so change would be another puzzle for the interested student.

Advantage was taken of the prepared tables to enquire into the following additional questions which it was thought might possibly have some bearing on the movement of the axis:

What is the percentage of the cases examined in which the amount of the astigmatism differs in the two eyes? The answer is 25.5 in the hypermetropic, and 24.3 in the myopic cases; and there appears to be no special inclination towards this difference at any particular age, which perhaps tends to support the contention that the amount of astigmatism does not generally show a tendency to change with years. This question does not seem to have any bearing upon the change of axis. But there is a somewhat interesting gradation noticeable in the percentage of hypermetropic astigmatic persons whose axes differ in the two eyes. If axes are changing it is reasonable that they need not change precisely with the same rapidity in the two eyes. Forty-one per cent. of such cases occur in my tables, and the figures progress from 15 per cent., during the first two decades combined through 37 per cent. for the third, fourth, and fifth decades, to 40 per cent. for the sixth, and 50 per cent. for each of the remaining seventh, eighth, and ninth decades. In the comparatively few myopic cases 52.5 per cent. show a difference of axes in the two eyes, but without a regular gradation from one decade to another.

The question of ætiology inevitably arises. Why does the astigmatic cornea generally begin its life with one particular curvature? Is that due to the *clignement*, to the pressure of the lids? Would such hypothetical pressure continued throughout life in the same direction explain a varying axis? Or does the curvature antedate the pressure? Is it then due to some slight developmental irregularity in fetal life?

And how explain the rotation of the axis? Is it the resultant of two forces continuing throughout life, the lid pressure and another, the former being gradually overcome? Or is the effect of the lids a myth, and the rotation due to one force? And what might be that force? I think it must be the pressure of the lateral external muscles, exerted especially in such actions as those of reading. When one considers that in running through an ordinary novel of 350 pages the eyes make perhaps 12,000 double lateral movements, and that the serious work of many people entails such movements for many hours daily during the greater part of a lifetime, it does not seem absurd to suspect that the sedentary customs of modern life may tend in time to change the curvature of individual corneæ. It would

be an interesting task to compare the corneæ in this respect of readers and the illiterate, and also of those Eastern scholars the lines of whose books run vertically.

We are taking for granted that the astigmatism is purely corneal; but in this we may perhaps be assuming too much. While no statistics of my own cases have been collected their effect has been a strong impression that on examining lenses through fully dilated pupils one finds that a large proportion of the lenses of the later decades of life show peripheral opacities. Does the universal gradual sclerosis of the lens nucleus along with this tendency to vacuolation have a relationship to the changing axis? It would doubtless be going too far to conclude that by gradually changing the refraction and introducing a tendency to myopia slight peripheral cataractous formation is actually an attempt of nature to remove the disadvantage of presbyopia in relation to near work; but when the opacities develop slowly, as is very often the case, and do not obstruct vision, that is sometimes precisely what happens. Hence the oft-repeated story of persons who having had normal distance vision in youth and middle age when 70 or 80 read comfortably without glasses. But if we suppose that lenticular opacities produce a change in the nature of astigmatism, it has to be explained why it should so commonly be in one and the same direction, a greater puzzle than is provided by the hypothesis that the astigmatism is corneal.

DISEASES OF THE EYE DUE TO SYPHILIS AND TRYPANOSOMIASIS AMONG THE NEGROES OF AFRICA.[1]

By Dr. J. N. ROY, Physician to the Hôtel-Dieu, Montreal; Late Special Delegate of the Canadian Government; Laureate of the Academy of Medicine of France.

AMONG the many subjects for study, which have most interested me, during my last journey to Africa, where I visited twenty-two different colonies, were syphilis and human trypanosomiasis. If the geographical distribution of sleeping sickness is relatively easy to determine, since this affection had its birth in this continent, the same cannot be said of syphilis, which was imported at various periods, and introduced in manifold ways.

Much has been written of the origin of pox. However, it is not my aim to sum up the different theories here; I will content myself with merely stating the principal ones in connection with the subject I am treating.

According to the opinion expressed by Sydenham, Haller, and later by Sprengel (1796), Africa was the primary center of syphilis, which next came to Europe. In my opinion, this hypothesis is incomplete for, if I am ready to accept it in part, I must reject it as a fundamental idea. Indeed, it is generally admitted that Asia was the cradle of this affection, and that it existed in the East Indies from a very early date. The Ethiopians, and above all the Egyptians, in daily contact with the people dwelling on the coast of the Red Sea and the Levant, were naturally all exposed to the contagion. Moreover, the first Arabian conquerors, syphilized for a long time back, estab-

[1] Read before the Canadian Medical Association, Quebec, June, 1919.

lished themselves definitely in Northern Africa during the seventh century, by repulsing the Berbers or by mingling with them. In 711, the Moors invaded the south of Spain, which they occupied for more than seven hundred years, and during this period, bands of natives were constantly crossing the Strait of Gibraltar.

In Europe, we can say that the history of pox dates chiefly from 1493, the date at which Christopher Columbus returned from his first voyage to America. I will not discuss the opinions expressed on the probability of the importation or exportation of this disease by the sailors of the intrepid Genoese navigator. I will content myself merely with recalling that in South America, the specific lesions have been observed in the skeletons of Indians who inhabited the country before the Spanish conquest. Moreover, as I have already intimated in another article, to me the redskins are Mongols who crossed Bering Strait, and peopled this vast continent. And besides, it is admitted that the Chinese have been syphilitic for an indefinite period.

As we have been able to note, the negroes have not yet been brought into the case, and it is necessary to consult the most recent works in order to find a more precise hypothesis. Mühry (1856) thinks that syphilis was imported from tropical Africa to Portugal in the fourteenth century, during the reign of King Henry the Navigator. I am unable to share this opinion because, in all the Dark Continent, it is exactly in the periequatorial region that syphilis is least common, and its hereditary manifestations are exceedingly rare. Moreover, in the great forest, this affection was unknown before the arrival of Europeans. Without going further into details, I think that the long sojourn of the Moors in Spain, driven from Andalusia in 1492 by Ferdinand and Isabella, has contributed largely toward syphilizing this part of Europe, even before the return of Columbus.

I believe then that syphilis was imported from Asia to Northern Africa, and that the Arabs and the Berbers infected the Moors of Mauretania, who, in their turn, have transmitted their pox to the negroes with whom they came in contact.

The Ethiopians were contaminated in two different ways:

first by the Egyptians always at war with them, and next by the Arabs who, coming from Yemen, crossed Erythræ and the Somali Coast, and took possession of Harar, the capital of the country of the Gallas. Their very long stay at this place has left certain customs peculiar to their civilization, notably concerning women, and which we still find there to-day. H. Blanc is of the opinion that the Abyssinians were infected by the Portuguese during the fifteenth century. Surely at that period, syphilis already existed in Portugal, and had also for a long time back shown itself in Abyssinia.

From the mingling of the Fellahs of Egypt with the blacks, were born the Peuhls, who inhabited the region of Upper Senegal-Niger, and the Foulahs, who are met with especially at Fonta Djalon, in French Guinea. These Foulahs, called Fellanies in the English colonies, conquered and contaminated the powerful tribe of the Haoussas, localized in the neighborhood of Sokato and Kano in Nigeria.

It is interesting to note that these last-named blacks were acquainted with and actually practiced couching of cataract. This practice comes to them from the Fellanies, who themselves took it from their ancestors, the Fellahs of Egypt, where this operation has always been much esteemed.

These Peuhls, these Foulahs-Fellanies, and these Haoussas, races which are very nomadic, and very much infected with syphilis, have been of the highest importance as propagating agents in every spot they have traversed.

During my travels in this part of Africa, I noticed that the blacks connected with the Arabs, the Moors, the Egyptians, and their blends, have inherited not only pox, but also trachoma. This conjunctivitis is extremely common among the natives who inhabit the northern part of the continent, contrary to the opinion of Swan Burnett and certain other authors who believe that the negro is immune to it. Ocular and palpebral complications are as frequent and numerous among them as among other races who suffer from it, and in the desert this affection is, from every point of view, most serious. However, I should add that in all that part of Africa situated south of the 5° north parallel, trachoma is very rare, and in the great jungle it is absolutely unknown.

Angola was infected by the Portuguese, who have owned this

colony for over four hundred years, and Eastern Portuguese Africa has shared the same fate.

South Africa, the scene of numerous wars between the natives, the Dutch, the Boers, and the English, has seen its magnificent blacks rapidly become more and more contaminated, especially by the soldiers. However, I must say that the last Anglo-Boer campaign was the most fatal. This is easily explained, because it is recognized that in Europe three times as much venereal disease is found in the British army as in the others, and particularly syphilis. Moreover, it has been observed that after each war, a great recrudescence of this kind of disease is always shown. The Zulus, who are one of the handsomest and healthiest races of all Africa, knowing nothing of syphilis before the arrival of Europeans, have named it "the white man's disease." Civilization has not only brought the Kaffirs this gift, it has also bequeathed them tuberculosis, and nowadays they are often attacked by acute phthisis, contracted in the mines of Johannesburg or elsewhere.

As it is admitted that the yellow race suffers a great deal from pox, it would have been interesting to seek for syphilis among the Hottentots and the Bushmen, who have in their veins Mongol blood, as we have had occasion to say in a previous work. Unfortunately, it is almost impossible to reach and study on the spot a sufficient number of the natives of these two tribes, now almost extinct, and thus arrive at a conclusion. Moreover, the means of communicating with them are most difficult, since they inhabit the frontiers of Portuguese Angola, of Southwest German Africa, and the neighboring English possessions.

English East Africa was infected particularly by Hindoos imported from Asia, who are also met with in Zanzibar and in Natal.

Africa has been almost entirely divided between certain countries of Europe, who are endeavoring to obtain the greatest possible profits from it. In order to penetrate into the interior, they have constructed railways, and put boats on the waterways, and in this manner the contaminated negroes have not been long, on their journeys, in transmitting their diseases.

Another means of contagion has been the transport of syphi-

litic black soldiers from one colony to another in the same country. And if, to all which I have just said, I add the scattered cases of pox imported by Europeans, not yet named, we see that this affection has entered Africa by many different places.

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Sleeping sickness, on the western coast of the Dark Continent, is spread on a belt of approximately 30°. In fact, we begin to meet it in the St. Louis region—and it spreads to upper Senegal, even to Timbuctoo, on the Niger. From St. Louis, we find it again more or less frequently on all the south coast as far as Mossamedes in Portuguese Angola. The French Congo and the Belgian Congo, with their gigantic rivers, are particularly contaminated.

In the Oubangui-Chari-Tchad region, trypanosomiasis is spreading to Bahr-el-Ghazal, and the neighborhood of Lake Victoria-Nyanza has been infected by the Belgian Congo.

Since some years back, it has made it appearance in the northeast of Northern Rhodesia, as well as in the neighborhood of Lakes Nyassa and Tanganyika.

Uganda is the part of Africa where sleeping sickness has caused the greatest ravages.

. . . . . .

I have had occasion to examine and study in a special way one hundred and thirty-five negroes, of whom the diagnostic of syphilis had been made without question; and it is the result of my observations on the ocular alterations of this disease which I desire to describe to-day. Most of these blacks, seen here and there, were brought to me in the hospitals, and traveled sometimes a great distance in order to meet me.

Thirty-eight cases among them had a perforation of the nasal septum, or of the palatine vault, or of both at the same time, and twenty other cases presented other lesions of osteitis. These syphilitics had therefore been very severely infected. As for the others, there was nothing particularly interesting about them, except that I have noted among certain subjects a rather strongly pronounced alteration of the buccal mucous membrane.

As the negroes, in general, treat their syphilis rather carelessly, or delay a very long time before having it attended to,

I have been struck with the resistance which their eyes—and above all the deep membrane—presented to the spirochaeta of Schaudinn.

I can say the same thing as regards the spirochæta of Castellani, for in yaws, pustules can be found on the eyelids, but no diseases of the eye has yet been noted.

In the hundred and thirty-five cases of syphilis examined, I found ocular alterations only sixteen times, and with the exception of a single case, all the lesions were located in the anterior segment. There follows a very short recital of my observations:

CASE REPORT 1.—Amadou Diop, Oualofs tribe, man of 22 years, syphilitic since 10 months. Iritis of the right eye, V = $\frac{1}{10}$. Left eye normal, Em. V. = $\frac{8}{8}$.

CASE REPORT 2.—Sidiki Sidibe, Bambara tribe, man of 28 years, syphilitic since 1 year. Iritis of the right eye, V = $\frac{1}{8}$. Left eye normal, Em. V = $\frac{10}{10}$.

CASE REPORT 3.—Amala Niamia, Galla tribe, woman of 20 years, syphilitic since 11 months. Iritis of the left eye, V = $\frac{1}{10}$. Right eye normal, Em. V. = $\frac{8}{8}$.

CASE REPORT 4.—Makila, Haoussa tribe, man of 25 years, syphilitic since 2 years. Iridochoroiditis of right eye, finger at 3 metres. Left eye normal, Em. V = $\frac{8}{8}$.

CASE REPORT 5.—Lufungula, Batanga tribe, man of 31 years, syphilitic since 5 years. Double chronic iridochoroiditis. Double consecutive cataract. Luminous perception.

CASE REPORT 6.—Fondia Kamara, Soussous tribe, woman of 29 years, syphilitic since 2 years. Consecutive cataract. Pupillary seclusion. Sub-acute glaucoma. No luminous perception. Right eye normal, Em. V = $\frac{8}{8}$.

CASE REPORT 7.—Fatima Ba, Peuhl tribe, woman of 45 years, syphilitic since 14 years. Chronic double iridochoroiditis. Double consecutive cataract. Luminous perception.

CASE REPORT 8.—Boumba, Fantis tribe, woman of 40 years, syphilitic since 11 years. Chronic double iridochoroiditis. Right eye, fingers at 2 metres. Left eye, fingers at 1.50 metre.

CASE REPORT 9.—Yaw Mensa, Ashanti tribe-man of 50 years, syphilitic since 30 years. Chronic double irido-choroiditis. Double consecutive cataract. No luminous perception. Perforation of the palatine vault and of the nasal septum.

CASE REPORT 10.—Akula, Haoussa tribe, man of 25 years, syphilitic since 1 year. Double iridochoroiditis. Right eye, fingers at 3 metres. Left eye, fingers at 2 metres.

CASE REPORT 11.—Agou Mabio, Bassa tribe, man of 38 years, syphilitic since 10 years. Chronic irido choroiditis of the right eye. Consecutive cataract. Luminous perception. Left eye normal, Em. V = $\frac{12}{6}$. Perforation of the nasal septum.

CASE REPORT 12.—Bakary Koulibaly, Bambara tribe, man of 22 years, syphilitic since 2 years. Double disseminated choroiditis. Right eye, Em. V = $\frac{1}{6}$. Left eye, Em. V = $\frac{1}{10}$.

CASE REPORT 13.—Simono, Crooman tribe, boy of 17 years, hereditary syphilis. Chronic parenchymatous keratitis of the right eye. Left eye normal. Right eye, Em. V = $\frac{1}{6}$. Left eye, Em. V = $\frac{12}{6}$.

CASE REPORT 14.—Kum Nibape Kum, Duala tribe, man of 28 years, syphilitic since 11 months. Parenchymatous keratitis of the left eye. Right eye normal. Right eye, Em. V = $\frac{10}{6}$. Left eye, Fingers at 2 metres.

CASE REPORT 15.—Isubi, Kumba tribe, man of 22 years, hereditary syphilis. Parenchymatous keratitis of left eye. Right eye normal. Right eye, Em. V = $\frac{8}{6}$. Left eye, Fingers at 3 metres.

CASE REPORT 16.—Koko Ayaba, Macua tribe, woman of 19 years, hereditary syphilis. Double chronic parenchymatous keratitis. Right eye, Em. V = $\frac{1}{6}$. Left eye, Em. V = $\frac{1}{10}$.

In order to explain the very good vision of the healthy eye met with in some of the preceding cases, I shall repeat what I have already set forth at length in an article, namely that visual acuteness is better among negroes than among all other races.

In short, among one hundred and thirty-five syphilitics, I have seen three cases of iritis in the acute stage; eight cases of chronic or acute iridochoroiditis; four cases of parenchymatous keratitis; and a single case of disease of the fundus of the eye where the choroid was affected. I have never observed condyloma or gummata of the eyelids or of the iris, although it should all the same be met with from time to time.

The retina has always been found healthy, and the negroes, in a general way, are very little exposed to albuminuria, diabetes, leukæmia, or other diseases which ordinarily produce an alteration of this membrane. This is perhaps due to the fact that they live continually in the open air, that they have no moral cares, and that their food consists almost entirely of fruits, cereals, and vegetables. When they eat meat, they are accustomed to boil it so much that it no longer contains toxins, and the little alcohol they make and drink is harmless.

Paralysis of the ocular muscles has likewise never been noted, nor has optic neuritis.

I desire now to bring to your attention locomotor ataxia and the gray atrophy following. After a most thorough investigation I believe I am in a position to state that there is, as yet, no tabes among the African negroes. The disease is almost exclusively the endowment of the white race, as I have never met it among the Malays or the three thousand Redskins which I have examined in the two Americas. It is moreover excessively rare among the Asiatic Mongols, as well as among the Hindoos whose ancestors were Aryans. The negro, having no intellectual preoccupations, is not exposed to nervous affections, central or spinal, and with him, the most serious manifestations of syphilis are the lesions of osteitis. Moreover, as he perspires a great deal, and as he is constantly exposed to the sun, with very little clothing, his irritated skin is quite often affected.

The mulatto, on the contrary, is as predisposed as the white man to diseases of the brain and of the spinal cord, and it is, indeed, astonishing that a single intermixture can produce among the blacks, such important affects from the point of view of diathesis. We have likewise noted the same thing among the other half-breed.

If the proportion of iridochoroiditis appears, at first sight,

to be rather high, this is because my arrival in the different centers becoming quickly known to the natives, they willingly brought the blind of their locality and its environs for my advice, and I, for this reason, examined the most serious cases.

From the observations which I made in Africa, I can say, with Dr. Santos Fernandez of Cuba, that the eyes of the blacks are very rarely affected in pox. This is contrary to the opinion of Dr. Pollot, who declares that negroes are strongly predisposed to syphilitic ocular diseases. It is probable that our American confrère intended to speak of the mulatto, not differentiating between him and the negro, when in reality, from a pathological point of view, an enormous difference exists. As already mentioned, a great number of my cases were very seriously infected, and the larger number had never received treatment. Moreover, I consider my statistics not absolutely exact, since the blind especially were brought to me, and then the diagnostic of syphilis was made. If, on the contrary, I had examined all those having pox in any district, I am sure that the percentage of ocular affections would have been less than that given in this article. The fact that I have met with a single case only of diseases of the fundus of the eye, is also an argument in favor of this hypothesis.

After having, here and there in Africa, studied syphilis and its manifestations of every description, I am disposed to believe that certain tribes are now immunized. The affections observed among the blacks of these tribes, are in general trifling and the bony lesions are extremely rare. However, woe to the other races infected by them—and especially the white—for, at that moment, the disease breaks out with a great virulence. Moreover, we know the pox has a particular degree of gravity when it is transmitted to a race primitively free from it. For example, in French Guinea, I have come in contact with a large number of Soussous recently contaminated by the Foulahs, of the Fouta Djalon; in Nigeria, some Yoroubas and Egbas, infected by the Haoussas; and finally on the Coast of Somalis, some Issas, Somalis, and Danakils, syphilized not long ago by the Ethiopians, showing large perforations of the roof of the mouth, or of the nasal septum. In other cases, syphilis was localized in the bones, and especially in the tibia. While traveling in Asia, and in South America, I have been equally

impressed by this phenomenon of immunity among the Chinese and particularly among the Redskins.

According to Livingstone (1857), the pox would not persist under any form among the native pure blood races of Central Africa, but on the contrary, will manifest itself among half-breed populations. The authors who mention this opinion, think that if this fact was verified by a long observation, it would have to be admitted, the immunity depended on the race much more than on the climate. In my opinion, this great explorer, Scottish Missionary, was impressed by the large number of syphilitic mulattos found in the great cities of South Africa. Once in the interior of the country, seeing no longer this affection, he would have come to the conclusion that the blacks, living in the center of the Dark Continent, were more or less refractory to it, and that among them syphilis would always heal without leaving any traces. Useless for me to insist on the fact that such is not the usual course of the pox. Furthermore, this disease was not widespread among the natives of the great forest before the coming of the European, and even now, could very seldom be found. As far as immunity is concerned, I willingly admit its existence, but only among the races syphilized for many generations, and the climate would have nothing to do with it. And moreover, I believe this immunity can be found among all races.

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Medical literature already describes a certain number of cases of affections of the eyes in human trypanosomiasis. Thiroux and d'Anfreville de la Salle, having had under observation four blacks with oculary troubles, expressed themselves as follows: "In the first case, the matter was a diminution of visual acuity with hemeralopia and very violent pains of the eyeballs, in a patient who had never taken any atoxyl, and who had a quite severe œdema of the papilla. The treatment, which we feared to apply in this case, caused the accidents to disappear in a few days."

"In the other two cases, we have observed iridocyclitis; in one case, the inflammation of the iris rapidly disappeared under the influence of the medication; in the second, the disease was more tenacious, and lasted about three weeks, causing some small posterior synechia, though atropine had been used.

With this patient, iritis had been preceded by phlyctenary conjunctivitis, and by small lesions of ulcerous keratitis which had cured rapidly enough under the influence of calomel dressings.

"The fourth patient was suffering from widely spread chronic keratitis, the intensity diminishing at the dressing period, and becoming more acute at the relapse. The variations were specially rendered more sensitive by the more or less opaque appearance of the cornea. In man, this keratitis, though having a less rapid course, resembles very much the one so often found in trypanosomized animals."

Doctor Heckenroth, in a conversation told me of having treated a sharpshooter of forty years of age, of the tribe of the Malinkes, for a parenchymatous keratitis of the right eye, dating back to four months. This black—who was not a syphilitic—recognized to be afflicted with sleeping sickness, was injected with 0.75 centigrammes of atoxyl. This injection improved his sight considerably. At a later period, the patient during eight days, took 0.75 centigrammes of orpiment in pills every twenty-four hours, and two weeks after the beginning of the treatment, he was perfectly cured of his keratitis. Before going to the capital of the French Congo, I have met this sharpshooter—Bakary Kamara—who was in Doctor Thiroux' ward, at St. Louis of Senegal. Though he had been sick for two years and a half, his general condition was still satisfactory enough, his cornea were perfectly transparent and his emmetropic eyes had a vision of $\frac{8}{8}$ each.

To my knowledge, seven observations of affections of the eyes, in human trypanosomiasis, have been published in Europe. Unfortunately, some of these observations are incomplete, since in certain cases these oculary troubles are described in a very indefinite way, and in others, no examination of the fundus had been made.

Dr. Morax, in a series of very interesting and well documented articles, has exposed the pathology of the eye in sleeping sickness and trypanosomiasis of other varieties.

In Africa, having examined, in different hospitals and concentration camps, four hundred and eighteen blacks, affected by this terrible disease, I will relate briefly what I have found out regarding their eyes. In the first place, I will say that the alterations of the eyes of the natives of this continent are most

uncommon in trypanosomiasis. Out of this number of cases, which are numerous enough, I have hardly found three cases showing trouble of the fundus, and even then, the etiology was doubtful, as I am now about to show.

CASE REPORT 1.—Ikolo, Mongo tribe, woman of 22 years. This patient has suffered from trypanosomiasis for a year and a half. Within two weeks, she developed a diminution of sight. At present, she is given hypodermic injections of atoxyl. She is not syphilitic. This woman complains of violent headaches, and shows signs of meningitis. The general condition is bad. At the examination of the eyes, I found a double œdematous papillitis. The veins of the retina are dilated, but there is no hemorrhage. No dischromatopsy. The sensitiveness of the conjunctiva is preserved. The other parts of the eye are normal. Due to the apathetic state in which I found the patient, it is impossible for me to make a refraction.

CASE REPORT 2.—Lokongo, Batetela tribe, man of 24 years. For two years suffering from sleeping sickness. Was always treated with hypodermic injections of satoxyl. His vision diminished within ten days. Has never contracted syphilis. Intense cephalalgy, and menigitis. General condition very bad. Ophthalmoscopic examination reveals a double œdematous papillitis. Dilatation of the veins of the retina, without hemorrhage. Colors are easily seen. Conjunctiva has retained its sensitiveness. Good pupillary reaction. The other parts of the eye are normal. As in the above preceding case, I cannot obtain any information about his refraction.

CASE REPORT 3.—Sakana, Ababua tribe, woman of 23 years. This patient is infected for a year. Was treated first of all with atoxyl. Satoxyl is now given to her in hypodermic injections. A month ago, when admitted to the hospital, on the 6th of February, 1913, this woman was complaining of a diminution of visual acuity, of headaches, and was, it seems, showing signs of meningitis. No examination was then made of the fundus of the eye. She is not syphilitic. Her general condition, under the influence of this treatment, has greatly improved. The examination of the eye has shown a slight double œdematous papillitis, with a small dilatation of the veins of the retina, without hemorrhage. Colors are well recognized. Conjunctiva has retained its sensibility. The pupil reacts well. The other oculary mem-

branes are in normal condition. Her refraction gives: Right eye, Em. V = $\frac{1}{3}$. Left eye, Em. V = $\frac{1}{3}$.

In my first two observations, the patients, in extremis, were really showing signs of meningitis, and pupillary œdema could have been just as well brought on by an increase of cephalo-rachidian liquid than by a direct infection of the trypanosoma.

In my last case, having made but one examination, it has been impossible for me to follow the evolution of the trypano-somiasis, and the consequences of his papillitis. Nevertheless, under the influence of a satoxyl treatment, the general symptoms and the visual acuity were rapidly improved,—without lumbar puncture—so this time, I believe to be in presence of a case of papillitous œdema, brought by trypanosoma. I would point out that the first observation of Thiroux and d'Anfreville de la Salle, is similar to mine, as far as the papilla is concerned. Also, until the microscope has settled the question of the presence or absence of this specific agency in the anatomical lesions, we will have to content ourselves with hypothesis.

The excellent visual acuity of the blacks affected by trypanosomiasis, has always impressed me, and in Belgian Congo, I even observed, in a boy of 18 years old, of the Basoko tribe, a vision of $\frac{20}{5}$.

According to me, the asthenopia of the eye, observed on certain subjects, in the last period, would be caused by the apathetic state in which they are before death—and which is characteristic—than to a special oculary manifestation in the sleeping sickness.

The sign of Argyll-Robertson has never yet been seen.

In my four hundred and eighteen patients, I have found nineteen white atrophies of the optic nerve, all following a treatment of atoxyl, or other arsenical salts. However, this does not present a great interest, since this toxic atrophy is very well known.

I never had the occasion to meet cases of palpebral œdema, iritis, cyclitis, iridocyclitis, parenchymatous keratitis, chor-oiditis, and chorioretinitis, such as mentioned by the authors who have made a study of the sleeping sickness. This is probably due to the fact that nearly all the subjects examined were under the influence of a treatment which had, more or

less, sterilized them, and as a consequence, all ocular complications had relatively cleared up.

If we compare the published observations, we see that the percentage of affections of the eye, in human trypanosomiasis, is far greater among the Europeans than among the blacks. The period of incubation is also shorter with the first named, than with the last.

Since the same objective symptoms are observed with those afflicted with oculary lesions, in sleeping sickness and in syphilis, and since a certain parallel can be established between these two affections, I believe that the eye of the black offers a greater resistance to the trypanoma than to the spirochæta.

The trypanosomiasis found in Brasil does not seem to give ocular manifestations; nevertheless, from time to time, palpebral œdema is found.

To sum up, I will say that Africa has not been the cradle of syphilis. This affection coming from Asia, has first ravaged the populations of the northeast and the north of this continent, and then has been transmitted to the blacks. Later on, at different epochs, the pox has shown up on the coast, brought over especially by the Europeans.

In sleeping sickness, alterations of the eyes are seldom met with in the blacks of Africa.

With them, this organ resists very well to this infection—and much more than with trypanosomized animals, who often show oculary lesions.

In syphilis, the affections of the eye are most frequently found in the anterior segment, and is less frequent with the blacks than with the whites—as also observed in human trypanosomiasis.

The nervous system of the blacks appears to have never presented any specific manifestations.

Some African tribes seem to have a certain state of immunity against the pox, which is very slight with them, and this immunity has already struck me in Asia, and in South America.

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SYMPATHETIC OPHTHALMIA. REPORT OF A CASE SUCCESSFULLY TREATED.[1]

By Dr. ALFRED WIENER and Dr. ELLIS BONIME, New York.

SURGICAL—DR. ALFRED WIENER.

WE are all familiar with the outcome of most cases of sympathetic ophthalmia. In spite of treatment, and attempts at operative procedures, the recurrent inflammatory attacks which take place defeat all our efforts. The patient ultimately becomes blind. It is especially the plastic types which offer such grave prognoses. Any treatment which will enable us to save the vision, or even restore it to a serviceable form, is surely worthy of record. It was just such a case that came under my observation about twelve years ago. Every effort had been made to prevent these recurrent attacks, but it proved futile.

When I saw the patient for the first time in 1907, he gave me the following history: Briefly related, ten years previous to the above date, he had injured his left eye with a scissors. About six years later the right eye suffered, after being hit with a baseball. From the date of the first injury, there were judging from the patient's description, recurrent attacks of iridocyclitis in the left eye at various periods. After the sixth year, the right eye suffered similar attacks, undoubtedly precipitated by the injury from a baseball. The advice given by Dr. Herman Knapp at the time of the first injury to have the left eye enucleated was disregarded. Just previous to the time that he first consulted me, he had been put through a course of treatment consisting of inunctions, potassium iodide, sweats and local depletion, by Drs. Barkan and Sewall of San Francisco.

[1] Presented at Section on Ophthalmology, New York Academy of Medicine, October, 1920.

The suspicion expressed at that time was that the patient was suffering from sympathetic ophthalmia.

My first examination of this patient made in September, 1907, showed the following condition: The vision in the right eye was $\frac{1}{200}$, and in the left eye $\frac{2}{10}$. In the right eye the pupil was bound down, and an iris bombe existed. The pupillary space was closed by a thin membrane, and the vitreous was so hazy that no details of the fundus were visible. The tension was slightly raised. In the left eye the pupil was drawn up and in, and an anterior synechia existed. This was probably the result of the former injury. This pupil was also closed by a thin membrane, and the whole anterior segment of the eye presented all the ear marks of a former plastic iridocyclitis. Again on account of the hazy vitreous, nothing definite in the fundus could be made out. Both eyes had distinct deposits on the posterior surface of the cornea, with well-marked corneo-scleral injection. The patient was of the robust type. A complete physical examination made at the time, revealed nothing of any significance. He denied ever having had any venereal infection. The first question which arose at that time in regard to the treatment, was whether the left eye, which had received the penetrating injury, and was in all probability the exciting eye, should be removed. As the disease now existed in both eyes, and the vision was better in the left eye than in the right, and furthermore, as it was not possible to say whether the vision in the right eye could be improved, we decided to place the patient under vigorous treatment and watch the result.

I performed an iridectomy on the right eye. Placed it under atropine and dionin instillations. The patient was given hot packs with pilocarpine injections, heavy doses of iodide of potash and salicylate of soda, with daily free catharsis. On January 2, 1908, the vision in the right eye had improved to $\frac{3}{10}$ and in the left eye to $\frac{3}{5}$.

The fundus in the right eye could now be seen. The disk was distinctly blurred, and the evidence was sufficient to show that a low grade of optic neuritis existed. An examination of the fields showed no contraction to white or colors. There were a few depigmented spots just above and to the outer side of the macula. The fundus in the left eye was so indistinct that no details could be made out. Between January and June of the same year, without any visible or ascertainable reason, the process lit up several times in the left eye, and the vision was again reduced to $\frac{2}{10}$. During the period between 1908 and 1914, in spite of all treatment and cautious living, there were recurrent attacks alternating between the right and left eyes, and the vision was very

badly affected. In May, 1914, a rather severe attack occurred simultaneously in both eyes. The vision was very much reduced, but after treatment recovered itself in the right eye to $\frac{1}{18}$, but in the left eye remained at $\frac{1}{100}$. Attempts to establish pupils, in either eye at various times during the quiet intervals, resulted in failures. As rapidly as an opening was made, an attack would quickly follow and close up the gap with an exudation which obscured the vision. It was noticeable about this time, that these plastic exudations were insidiously closing up the anterior segments of both eyes. Likewise a band keratitis was making itself evident. During this critical period every effort was made to discover a possible etiological factor. Microscopical and chemical examinations of the blood were negative. A Wasserman and gonorrheal fixation test were made and also proved negative. Every effort was employed to discover a latent tuberculosis but none was found. Careful physical examinations with X-ray of the chest, nasal sinuses, and teeth, were made, but all proved negative. In spite of the fact that I personally felt that the left eye should be enucleated, no consensus of opinion could be arrived at. Its enucleation was refused as no definite promises could be made. A course of vigorous treatment was again decided upon. The treatment consisted in Hg injections, potassium iodide, hot packs with pilocarpine injection, sweats, vigorous catharsis, and massive doses of salicylate of soda, hot compresses with dionin and atropine instillations. The tonsils were removed, and the teeth carefully treated for suspicious foci. This treatment was kept up more vigorously when the attacks existed, and less so during the intervals. Again each time that I made a surgical endeavor to free the pupil in either eye, an immediate reaction took place, eventually defeating my purpose. February 10, 1919, the vision in the right eye was counting fingers at two feet, and in the left eye fingers at one foot. Tension was slightly minus in both eyes, measuring with the Schiotz 8*mm* of Hg, in the left eye, and 10*mm* of Hg in the right. The projection was good in both eyes. The band keratitis was more developed, and was occupying the central portion of the cornea in both eyes. In this desperate state, I was persuaded by the patient to make one more endeavor to obtain vision in the right eye. He was prepared most carefully, and given massive doses of salicylate of soda. In spite of this, an attempt to free the pupil was followed by so tremendous a reaction, that it was decided to give up all further attempts. The tension now was distinctly minus in both eyes, with fair projection in the right, and very poor in the left. In the right eye the anterior chamber was fairly normal in depth. The iris was discolored and atrophic. Its

natural folds were obliterated. It appeared to be firmly bound down on the lens, and the pupillary area was closed by a rather thick membrane. A similar condition existed in the left eye but more exaggerated in type. The vision taken in the early part of September, 1919, was light perception in both eyes, and hand movements excentrically toward the right in the right eye. The patient was helpless, and had to be led about.

About this time I became acquainted with a method of treatment for chronic joint diseases, for which vaccines were given intravenously and subcutaneously. A colleague of mine practicing orthopedic surgery had been very successful with this class of cases, by allowing his patients to undergo a course of such vaccination. The theories upon which this vaccination were based were explained to me by Dr. Bonime. His method of therapo-immunity appealed to me at once, and I was anxious to make a trial of it in my patient. Of course a chronic joint is something very different from a chronic inflammation existing in an eye. Personally I have always been inclined to believe in the theory, which admits that sympathetic ophthalmia owes its existence to an infection pure and simple. Here was a method which dealt directly with this theory, and might give the results hoped for. I felt, that if in plain words, the patient could be sterilized, we might either prevent these plastic exudations from recurring, or if they had occurred, be able to operate without a consequent reaction destroying our result. In this case there was nothing to be lost and everything to be gained.

The patient was taken in charge of by Dr. Bonime. According to the method pursued by himself, a course of vaccination was given intravenously and subcutaneously. During this course of treatment I watched the patient very carefully for any exaggeration of his local symptoms. In the beginning of the treatment they were slightly more intense than they had been, but never so severe that it was necessary to interrupt the treatment. The patient experienced really very little local discomfort. The general reaction which was quite severe will be explained by Dr. Bonime. After six weeks the patient was ready for operative interference. As the tension in the left eye was decidedly minus, and the projection very poor, and there appeared to be no chance to better the vision in this eye, I decided to confine my efforts to the right eye. The tension in the right eye was practically normal, and the projection perfect. The vision was confined to hand movements. In order first to test out the eye, I made an attempt to perform an iridectomy. I was able to get away only a small piece of an atrophic iris. I waited one week and not the slightest reaction occurred. I then pro-

ceeded very cautiously to free the pupil from the underlying lens. Then the lens was removed by discission. It took several procedures to accomplish this. Not one of these attempts was attended by the slightest reaction, at once a proof that the infection must be under control. After the removal of the lens, I was confronted by a whitish looking exudate which existed in the vitreous just behind the lens. At first I tried to cut through it. This was found impossible without exerting too much pull upon the ciliary body. I finally, after several procedures with very sharp and fine needle knives, succeeded in separating it from its upper attachment. Gradually I procured an opening sufficient for the patient to obtain the first glimpse of vision he had had since one year. This has gradually improved since the last operation which was performed in April of this year. His vision taken on July 30, 1920, was $\frac{8}{10}$ with a +10 sph. = +0.75 cyl. ax. 15° N. The tension was normal and the projection perfect. The patient was going to his place of business and transacting ordinary business. He recently informed me that he played a game of golf. On taking his vision October 16, 1920, I find that with a plus 12 sph. in combination with a cylinder plus 1.50 axis 15° nasal he sees $\frac{15}{10}$. I don't think it is necessary to dilate upon the feelings of this patient, who just ten months previous had been pronounced not only by myself, but other colleagues, as a hopeless case.

Remarks. In view of the fact that a result was obtained in a case of sympathetic ophthalmia such as we rarely meet with, it is only fair to discuss the question, whether this is a true case of sympathetic ophthalmia, or what might be considered a relapsing chronic plastic iridocyclitis. I am in accord with Roemer, who considers the diagnosis of sympathetic ophthalmia only an apparent diagnosis. We know that sympathetic iridocyclitis is not characterized by any clinical specific peculiarities. This same clinical picture might be produced by the greatest variety of inflammatory excitants. We have no biological reaction which is characteristic of such a condition. Thus we are greatly handicapped at times in trying to prove that such a condition actually exists. It seems to me, however, if through careful clinical and serological examinations, all reasons for any other form of iridocyclitis have been excluded, this is surely one point in favor of the sympathetic type. If to this is added the history of a perforating injury to the globe,

followed by a chronic plastic uveitis, especially of the insidious type leading to an ultimate loss of vision, I believe we have the right to assume, that such a case should be classed under the division of sympathetic ophthalmia. Another convincing argument seems to me to be the fact that, previous to the immunization, every attempt, when the eyes were quiescent, to create a pupil, in which of course it was necessary to deal with the iris, resulted almost at once in a reaction in both eyes. After the immunization, no more attacks occurred. That there should have been such a long interval between the involvement of the first and second eyes, can, I believe, be accounted for, by the fact, that this patient was under constant observation and treatment, most of the time, by men who recognized the gravity of the first injury and feared the consequences. The second injury, one might well expect, would precipitate just such an attack, where we have a right to assume that the predisposition existed.

As I did not wish to tire the reader, with a recital of all the clinical manifestations as they occurred during the various attacks, nor the finer details of the operative procedures, considering them unimportant, I have refrained from being more explicit. This report is simply made to acquaint my colleagues with the fact, that I believe we may have at hand a method, which will assist us in preserving the vision of not only serious cases of sympathetic ophthalmia, but also those intractable cases of recurrent iridocyclitis, in which a somewhat similar pathological destruction of the anterior segment of the eye takes place. Probably if treated early, when the first evidence of a recurrent inflammation is apparent, all such conditions might be arrested, no interference of vision take place, and all operative procedures avoided.

IMMUNO-THERAPY—DR. ELLIS BONIME.

A careful study of the literature, substantiated my original conviction, that this is the first time that the combination of specific and non-specific immuno-therapy has been applied in the treatment of sympathetic ophthalmia. That being the case, it will be in order to give the details of the inception of the treatment, even though running the risk of appearing trivial.

Dr. Leo Mayer, the orthopædic surgeon Dr. Wiener referred to in his paper, had just been observing the result obtained with combination of non-specific and specific immuno treatment of subacute and chronic joint conditions, when the case under discussion this evening came to his notice. His sympathy was aroused sufficiently to make him call on me, to see if in some way the patient could be benefited by vaccine treatment. I was extremely skeptical, but knowing very little about sympathetic ophthalmia, I suggested consultation with Dr. Wiener. At this consultation, I questioned Dr. Wiener very carefully, with the view of ascertaining whether it was remotely possible to place sympathetic ophthalmia in the category of infectious disease, or whether at least part of the pathology might be due to a low-grade infection. Dr. Wiener's opinion was that sympathetic ophthalmia might have an infectious basis, but that up to the present time, nothing to substantiate this theory had ever been discovered by either the pathologist or the bacteriologist. However, as the history of the case was one of severe reaction, inflammatory in character, following every attempt at surgical interference upon the eye, there was sufficient evidence in favor of a bacteriological etiology, to justify, in a desperate case like this one, what may seem drastic treatment.

A thorough test with tuberculin excluded tuberculosis. Then I proceeded to treat the patient in the same manner as I would a low-grade chronic joint infection, popularly known as rheumatism. I used typhoid bacillus vaccine intravenously, in preference to any other foreign protein, because of its easily measurable quantities, to obtain the non-specific protein reaction, and an autogenous streptococcus, obtained from the tonsilar region for the specific immune-response. In this particular case, however, on account of the susceptibility of the eye to the pneumococcus, I added an autogenous pneumococcus vaccine, obtained in the same manner and at the same time with the streptococcus.

Beginning with twenty-five million typhoid bacilli intravenously, I produced a very severe chill, followed by a rise in temperature to 104. Three days later, I repeated the same dose of typhoid bacillus, but increased the subcutaneous streptococcus injection to one hundred and fifty million, The chill was not pronounced, and the rise in temperature was only

to 102.8. Four days later I increased the intravenous injection of typhoid bacilli to forty million, and the subcutaneous injection of streptococcus to 175 million. This time the chill was not very marked, and the temperature rose only to 102, despite the greater dose.

After a three-day interval, I again increased the dose, giving bacillus typhoid, 75 million intravenously, and pneumococcus, 200 million subcutaneously. This administration was followed by chilly sensations, lasting about an hour, but no distinct chill, and a rise of temperature of 103. The same dose repeated five days later, produced only a slight chill, and a temperature rise to 101.4. After an interval of another five days, the same dose repeated again, produced no chill and a temperature of 100.2. Three days later, the same dose produced no reaction. I then continued the subcutaneous injections of streptococcus and pneumococcus, administering 200 million streptococcus, and 250 million pneumo, increasing the dose to 225 million streptococcus, and 275 million pneumococcus a month later. Then again, about two weeks before the operation, 275 millions each of streptococcus and pneumococcus were given, and three days before the operation 300 million each were given.

Every intravenous injection was followed by a careful examination of the urine, especially for blood. On no occasion did we find occult blood present, and only once, a few red blood cells microscopically were found, and these we did not consider sufficient to interfere with the treatment. The presence of a macroscopic amount of blood would have been an indication for a longer interval between treatments, and a much more gradual scheme of dosage.

The mystery surrounding the defensive mechanism of the human body against invading pathological bacteria, is still so profound, that any explanation we can give regarding the observation made during the treatment, and the results obtained, can at most be speculative. But basing my conclusion on the most recent observations made by authorities on immunology, I formed the following theories:

Chronic infection may be the result of equilibrium established between the action of the bacteria on the one hand, and the immune response on the part of the individual on the other; or it may be the acquisition on the part of the organism of im-

munity against the action of the antibodies. Sometimes, such a status quo may be due to a deficiency of complement in the blood serum.

Most of you have probably observed that during the process of an acute infection, a present chronic infection, even of very long standing, will often disappear with the acute infection. An injection of foreign protein intravenously, produces a severe reaction, consisting of a chill, rise of temperature, profuse sweating, etc., simulating an acute infection; and like an acute infection, it rouses all of nature's latent mechanism of defense.

During this reaction, a superabundance of complement is formed, which completes the immune response against the organism causing the chronic infection, or aid in the therapeutic effect of the vaccines used.

In the case of sympathetic ophthalmia, it may also be possible that the repeated production of the protein reaction with the typhoid bacillus to a point of tolerance, may render the individual temporarily, at least, "reaction-proof."

Under the first theory, we have cured the chronic infection in the eye, making the surgical procedure possible; under the second theory, we render the patient "reaction-proof" for a time, at least, making surgical intervention possible without reaction. But whether you accept either one of these theories, or whether you reject both—I trust you will pardon my theorizing at all, in view of the practical, and I believe, far-reaching results obtained.

CYCLOPIA, ITS BEARING UPON CERTAIN PROBLEMS OF TERATOGENESIS AND OF NORMAL EMBRYOLOGY; WITH A DESCRIPTION OF A CYCLOCEPHALIC MONSTER.

By Dr. EMORY HILL, Richmond, Va.

(*Concluded.*)

(*With four illustrations in the text.*)

Histologic Examination.—The entire specimen had been preserved in formalin. The orbital contents were dehydrated in alcohol, embedded in celloidin, and sectioned serially from top to bottom, the sections varying from 15 to 20 microns in thickness. Tissues were treated similarly from the proboscis, the fungus-like growth on the head and back, the lids, the internal ear, and the abdominal organs which showed peculiarities. The lid tissue was embedded in paraffin. The following stains were used: hæmatoxylin and eosin, phosphotungstic acid hæmatoxylin, van Gieson, Pal-Weigert, toluidin blue, Golgi, and Mallory's neuroglia stain.

In the lids and conjunctiva, no abnormalities were seen except the absence of puncta and canaliculi and caruncles. The conjunctiva was devoid of adenoid tissue, as one would expect in the fetus and new-born infant.

The corneas showed a decided difference in development, the right being thicker than the left and having its layers better differentiated. The central portion of each cornea was very thin, measuring 132 microns in the center of the right cornea and 91.3 microns in the center of the left. The thinning took place abruptly at the lateral sclero-corneal junction in the case of the left cornea, but was more gradual in the right

so that only about one half of the diameter of the cornea was excessively thin. The median portion of the two corneas passed gradually into the intervening sclera which was likewise very thin. An occasional blood vessel was seen in the periphery of the corneas. The epithelial layer was absent over most of the surface. In a few sections it was four cells deep; more often one or two cell layers were seen. Exposure and possibly trauma may explain the scant epithelium. Only at the far periphery was there an approach to the adult thickness of this layer. The left cornea was more denuded of epithelium than the right. Bowman's membrane was well developed only at the lateral periphery of the corneas. Its maximum thickness was 11.4 microns. It gradually thinned and disappeared shortly median to the iris angle. The left cornea showed a poorer development of this layer than the right. The substantia propria was imperfectly differentiated from the sclera, having a less regular disposition of its lamellæ than normal. Its greater richness in nuclei, as compared to the adult cornea, is to be expected in the fetal eye. The staining of the substantia propria by van Gieson's method indicated well its poor differentiation. It stained almost as deeply as the sclera, whereas normal cornea stains much less deeply. The deeper staining characteristic of ordinary connective tissue was more evident in the left cornea. Descemet's membrane was exceedingly thin where visible, and in most sections was not seen. The endothelium showed as a single layer of cells in the right cornea in most sections, but was not usually distinguishable in the left cornea from a non-cellular granular deposit upon the posterior corneal surface.

The sclera varied much in different areas. The portion intervening between the two corneas was highly vascular and thin, measuring less than ¼ millimeter. The lateral portions adjacent to the corneas bulged into a connective tissue mass 3.5 millimeters in width. This area corresponded to the rounded and rather sharp border of the protruding, flattened anterior segment of the globe already described. Schlemm's canal was seen in the lateral portions but was absent in the median sclera between the corneas and in the upper and lower quadrants. The posterior segment of the sclera was of normal width.

The anterior chambers were shallow and free of abnormal

contents with the exception of a granular coagulum adjacent to the cornea. The iris angles were of the normal late-fetal type.

The irides were poorly developed in their lateral halves, and very rudimentary in their median halves. No muscle tissue was made out. No pupillary membrane was seen.

The ciliary bodies exhibited similarly a better development in the lateral portions and were smaller in their median portions. The meridional fibers of the ciliary muscles were more conspicuous than the circular fibers. The crowded aspect of the structures where the two eyes were fused in the midline was in strong contrast to the freer development of the lateral portions of the eyes.

The chorioid was normal in the anterior portion. In the posterior portion it consisted of a broad layer which was composed chiefly of a very loose reticular structure becoming more dense as it fused with the sclera, and a vascular portion next to the pigment epithelium having engorged vessels which presented a fairly clear division into choriocapillaris and a large vessel layer. There was no pigment in the chorioid, the chromatophores not containing pigment granules in fetal life. The pigment epithelium was generally adherent to the chorioid though the retina was detached.

The lenses were very small but otherwise normal except for the position of the left lens which was entirely below the horizontal plane in the inferior half of the globe, and the absence of zonular fibers. The maximum diameters of the right lens were 5 x 3*mm*, of the left lens 4.5 x 2.5*mm*.

The vitreous chamber was much diminished in size. Its fetal characteristics were not observed; the vascular system was nowhere seen. The partial separation into two chambers was everywhere indicated by the two retinas and, in the lowermost portion of the globe, by an irregular tongue of connective tissue which ran antero-posteriorly in the midline. The rough division into two eyes indicated larger diameters and better development of the structures of the right than of the left segment. The less orderly development of the lower portion of each segment accords with the usual observation that cyclopean eyes fuse mainly in the region of the fetal cleft. No coloboma or colobomatous cyst was found, however, in this specimen.

The retinas were detached in most of their extent. In general they followed the contour of the vitreous chamber from the lateral ciliary bodies backwards to the region of the posterior pole of the eye and from there curved forward running parallel to each other towards the median ciliary bodies. In the upper half of the globe the retinas approached the normal appearance. The scant and small ganglion cells and the absence of a nerve fiber layer were the principal abnormalities. A more perfect arrangement of the retinal layers was noted in the anterior than in the posterior portion. Adjacent to the papilla there was much folding, giving an appearance somewhat suggestive of rosette formation. In this region the nuclear and granular layers were all excessively broad and in places poorly defined, presenting an edematous appearance. The same condition was observed here and there throughout the extent of the retina, more especially in the lower part of the globe. Occasionally cross-sections of retinal vessels were seen, which in a few instances were accompanied by a slight perivascular round-cell accumulation. No fovea was made out. The rods and cones were well preserved in places, but frequently they were indistinct. The more distorted portions of the retina showed a predominance of neuroglia. This was strikingly evident in sections stained by Mallory's stain. One hesitates, however, to state that there was an actual excess of neuroglia; it may be that the scantier nervous elements allowed the relative excess of supporting tissue to assume larger proportions without an absolute increase of this tissue. The special stain for neuroglia disclosed the fact that the similarity of the retinal folds to rosettes was only superficial. The ganglion cells were nowhere of normal size and staining properties. Nissl granules could not be brought out by the toluidin blue method. The position of this layer was occupied by small cells whose nuclei were similar to those of the inner nuclear layer, but stained less deeply with nuclear stains. Only rarely could a cell body approximating the size and shape of a ganglion cell be distinguished. No nerve fibers were made out with certainty. The position which they should occupy was either not filled or was assumed by neuroglia fibrils.

The optic nerve apparently was altogether lacking. The nervelike structure seen macroscopically was composed of

connective tissue and bore the central retinal vessels. This tissue was carried forward in the form of a tongue of mesoderm already mentioned as traversing the back part of the floor of the globe, indicating the partial division into two eyes.

The orbital tissues consisted of normal striated muscle and a large amount of fat. On each side of the globe, embedded in fat, were cross-sections of glands which correspond in structure to the lacrimal glands. This tissue was very scant; macroscopically no lacrimal glands were found.

The ciliary nerves were nowhere found; the blood vessels were abundant in the orbital tissues and the eyes, except for the scant retinal system; but these vessels could not be traced back to brain vessels. A few vessels were surrounded by a small round-cell accumulation.

The proboscis was composed of normal skin with hair follicles, sweat glands, fat, blood vessels, and a loose reticular subcutaneous tissue. The basal portion contained cartilage. The lumen was lined by stratified squamous epithelium. A few blood vessels were surrounded by round-cell accumulations. No olfactory nerves were found.

The mass of tissue occupying the head region was composed of thin-walled blood channels with a neuroglia framework and occasional cells which approximated the size and shape of nerve cells but showed no Nissl granules with the toluidin blue stain.

The decalcified petrous bone contained a normal cochlea with red blood cells in its cavity. No semicircular canals or nerves were found.

Interpretation of the Monstrosity.

The specimen described corresponds in general with the human cyclopean monsters reported in the literature. In the clumsy nomenclature of teratology it is an example of cycloexencephalo-rachischisis. The double character of the median eye with greater deformity in its lowermost part is the usual condition when the eyes reach a moderate degree of development. The damage to the brain and spinal cord is out of proportion to the damage to the optic vesicles. Cleland's (17, 18), observation is of interest in this connection. He found

that dropsy occurred later and caused more injury in cyclopia than in anencephaly. It is probable that the central nervous system in this specimen developed at first proportionally to the eyes but was later destroyed by a great accumulation of cerebro-spinal fluid with subsequent rupture. The fungus-like growth occupying the position of the brain shows that some differentiation into nervous tissue has occurred. That the vascular system has been developed in the head region is evident from the abundant blood supply to most of the orbital tissues, although no connection exists any longer between the great vessels of the neck and the ocular circulation. The possibility that an inflammatory process is responsible for the failure of development in this specimen is suggested by the round-cell infiltration about blood vessels in the retina, muscle cone, and proboscis; this is a very occasional appearance and of very slight degree.

The better development of the cranial bones on the right side and of the right segment of the eye is not in accord with the better development of the left carotid artery. Probably too much stress is laid upon a correlation of blood supply with the growth of embryonic tissues. An attempt to correlate the abnormalities in this specimen with Assheton's (4, 5) dictum that the superior growing point of the embryo gives rise to the brain, medulla, heart, and foregut, while all the rest of the body is derived from the inferior growing point, is not altogether successful. The central nervous system, including the eyes, was involved and the heart was very abnormal in shape; but the failure in development of the diaphragm, with the consequent displacement of the stomach and spleen, and the apparent absence of the suprarenal bodies, cannot be associated with the embryonic foregut. The chief abnormalities accord with Assheton's theory and also with Adami's (1) conception that cyclopia is a "superior polar hypogenesis," as will be explained later; but it is evident that the faulty development in this specimen is not confined to those parts dominated by the growth center of the head end of the embryo. In addition, the diaphragm has failed to complete its descent and the pleuroperitoneal membrane seems to have lagged behind, making with the rest of the diaphragm a compartment containing two organs which should have been in the abdominal cavity;

and the suprarenal bodies are not seen, as is very frequently the case in cyclopia. No explanation can be offered for the latter fact. Whether a defect in the cervical sympathetic ganglia is associated with the failure of the suprarenals could not be determined in this specimen because of the age and condition of the tissues.

The degree of development of the eye structures indicates that the fetus was at least seven months old. The most important abnormality is the practical absence of ganglion cells and nerve fibers from the retina and the mesodermal character of the optic nervelike structure behind the globe. The disputed question of the origin of these tissues will be discussed among the problems of embryology suggested by the study of cyclopean specimens. It is believed that the failure of these tissues is part of the widespread destruction of the central nervous system in human cyclopia and that it does not justify the theory that these tissues depend upon the optic centers in the brain for their growth. It is noteworthy that the retinal circulation is scant and the retinal layers deriving nutrition from this circulation partly failed, whereas the other ocular blood supply is abundant.

The median face structures are entirely absent except for the scant cartilage and the equivalent of a single nasal cavity in the proboscis. The olfactory nerves are absent, as are all the other cranial nerves. The mouth does not show a triangular shape as Dareste thought it must inevitably do in cyclopia. The high degree of normal development of the body in general, aside from the head, back, and upper portion of the face, bears out the impression that there was an early evolution of the central nervous system which was subsequently destroyed by hydrocephalus.

VIII. MODERN EXPERIMENTAL TERATOGENESIS.

The third stage in the modern history of teratology, according to Piersol (91), is by far the most important period, in that it marks the removal of many problems from the realm of speculation to the realm of fact. Probably no question concerning monstrosities illustrates this better than the question of the origin and meaning of cyclopia.

The early experimental methods of dealing with chick embryos have been described. Further investigations by Driesch (22) and Loeb (61), using the sea-urchin eggs, of Schultze (96) with frog eggs and of Wilson with amphyoxus eggs proved that double monsters can be produced by mechanical and chemical means. Mall (63), Becker (12), and Stockard (115) have described at length the various experiments of Von Pflüger, Roux, Born, Hertwig, Spemann, Morgan, Schaper, and others who have dealt with general problems of teratogenesis. Certain experiments especially interest the student of cyclopia. The addition of chemicals to the sea water in which fish embryos are grown gives rise to a variety of monsters. Herbst (35) found that lithium salts caused the blastoderm of the sea-urchin eggs to invert; Morgan (75) made the same observation upon frog eggs. Loeb (62) using a 1.5% aqueous solution of potassium chloride in the sea water in which he grew fundulus eggs, noted that the heart, though developed, did not beat, and the blood vessels had an irregular lumen like a chain of beads. He considered this condition due to a lack of normal blood pressure. Similar conditions are found in human embryos, according to Mall. Morgan and Tsuda (73) found that 0.6% sodium chloride prevented the closure of the blastopore, and a great number of monsters resulted. Hertwig (37, 38), using the same method, found delayed gastrulation and spina bifida in frogs. Similar delay in the closure of the anterior end of the neural tube produced anencephaly. This observation is of particular interest because it is precisely opposite to the theoretical explanation of Dareste, which has been discussed earlier in this paper, namely that a premature closure of the anterior cleft of the neural tube is responsible for cyclopia and the grave brain defects which accompany this deformity. Hertwig (38) found that 0.7% sodium chloride produced spina bifida in every case of axolotl (1896). This experience no doubt led Hertwig to the conclusion that every ovum has the power to become a monster, a dictum pronounced so emphatically by Mall in various contributions in recent years. Spemann constricted eggs of triton during the two-cell or later stages by a fine thread tied about the circumference of the first cleavage plane. Double-headed monsters with cyclopia resulted. Lewis (59), using fundulus eggs, pricked the anterior

end of the embryonic shield squeezing out some material by pressure after the needle was withdrawn. Little or no regeneration of nervous tissue occurred, and cyclopia resulted. Lewis believed that the eyes fused as a result of the absence of tissue which should lie between them.

Stockard's Experiments.

The remarkable contributions of C. R. Stockard between 1907 and 1913 taken together constitute an array of facts and logical deduction from facts which place cyclopia on a definite basis. Pursuing the plan of Hertwig, Morgan, and Loeb, Stockard (108, 109) utilized various metallic salts in varying proportions in sea water in which he grew the eggs of the teleost fish, Fundulus heteroclitus. Magnesium salts were the only ones which regularly produced a specific type of monster, cyclopia. Spemann (102) had already produced cyclopia in an amphibian (triton). Stockard (109) produced the first typical cyclopean fish (1907) and gave the first example of the consistent production of a vertebrate monster by changing the chemical environment of the embryo. By using an excess of magnesium chloride in sea water he produced cyclopia in 50% of his embryos (115). A $\frac{1}{11}$ molecular solution of magnesium chloride was the optimum proportion. Weaker and stronger solutions produced fewer cyclopean fish, showing that neither a chemical effect nor osmotic pressure is the cause of the monstrous development. Stockard (110) thinks the effect is toxic, the magnesium having an inhibitory or anesthetic effect which prevents the outpushing of the optic tissues. The cyclopean condition was evident in from sixty to seventy hours. The eggs were then placed in normal sea water, and continued to grow and hatch normally. All grades of cyclopia appeared, the eye being ventro-median looking forwards and slightly downwards. The embryos were normal except for the eyes, nose, and mouth. Some had a rudimentary eye and some no eye. Stockard emphasized the fact that the various degrees of eye defect were not different stages in an embryo, but represented different embryos. The cyclopean defect is foreshadowed in its final condition when the optic vesicle first separates itself from the brain. After separation of the normal from the cyclo-

pean embryos, the former never exhibited cyclopia later, though kept in the magnesium solution. No subsequent fusion of the two optic vesicles or cups took place after that time (time of the first appearance of the optic vesicles). The cyclopean fish hatched more slowly, but they appeared to see, and lived as long as the yolk sac lasted (ten days in two cases). The optic outpushings appeared at thirty hours, when the brain was still a solid mass of cells without a central ventricle. This is important in view of Dareste's theory, already quoted. All teleosts should be cyclopeans, if Dareste's theory were correct. Stockard refers, in this connection, to Spemann's observation of his cyclopean tritons with an open neural tube, which is likewise inconsistent with Dareste's theory.

In order to remove all possibility of acting upon the eggs before segmentation had begun, Stockard applied the magnesium solution at later times and found that he could produce cyclopia at the thirty-two cell stage. This effectually put an end to the theory of the germinal origin of this monstrosity.

Stockard (115) at this time (1909) corrected his earlier impression that "the fusion of the two components may take place at different periods," and insisted that "no fusion of the eyes takes place after they are once clearly given out from the brain." This statement deserves emphasis, for it marks a radical departure from the position held by preceding writers on cyclopia, a position to which even Spemann (106) appears to have returned recently. The great contribution of Stockard is the definite and conclusive proof that cyclopia is not a fusion of two eyes as a result of the loss of intervening non-ocular tissue; but a failure of separation of the original optic anlage with the result that non-ocular tissue cannot find a place to develop in the midline. One of the last words of Mall (64) before his untimely death was an enthusiastic statement of this positive contribution to exact embryologic knowledge which he credits to Stockard.

The question immediately suggests itself as to the explanation of the astonishing effect of magnesium salts upon the embryo. Stockard has avoided dogmatic utterances all through his writings. He merely suggests that magnesium is known to exert an inhibitory effect upon muscle tissue and to be anesthetic to both vertebrate and invertebrate animals.

He thinks that this anesthetic effect accounts for the lack of energy on the part of optic vesicles to push out to lateral positions, which in its end result is equivalent to a pressure from without. Pursuing this idea of anesthetic effects upon nervous tissue, Stockard (117) experimented with alcohol, ether, and chloretone, and found the latter two produced general retardation of growth, while alcohol and magnesium were more localized and specific in their action. Alcohol produced from 90% of 98% of abnormal eyes, usually cyclopean; only a few of the fish developed to hatching and could swim. In one series, 5% alcohol in sea water produced 146 ophthalmic monsters with only three fish with two separate eyes. It appeared that magnesium affected chiefly dynamic processes such as the outpushing of the optic vesicles. Only anesthetics produced eye defects in Stockard's experience. Other salts and sugar solutions failed.

Stockard's observations naturally give rise to speculation in regard to the possible production of monstrosities in the human embryo by means of substances circulating in the mother's blood. Hertwig (38) raised this question in 1896. Mall (63) and Stockard (114) suggested the possibility that the tendency of a woman to produce monsters might be lessened by correcting uterine disorders and removing toxins from the maternal blood. Beck (11) has advised against the use of mineral salts and alcohol in pregnancy. The older experiments of Chas. Féré (26), a pupil of Dareste, had the advantage of dealing with such teratogenic agents as might operate in the human body. He injected into the chicken egg solutions of various alcohols, tetanus toxin, toxins of swine plague, bacillus pyocyaneus and hog cholera, and products of human tuberculosis. All of these substances increased the number of monstrous embryos to a high degree, as compared to controls. He found a direct relation between the toxic and teratogenic power of these poisons. In general, the gravity of the defects increased with the intensity and duration of the disturbing cause. Agents which had a teratogenic effect on the embryo in an early stage had a pathologic effect in a later stage. This observation accords well with Mall's belief in the essential similarity of pathologic ova and small monsters. While the possibility of preventing monstrous births in the human race

by the application of experimental knowledge such as Féré and Stockard have contributed is not yet a reality, it is perhaps reasonable to hope that practical results may be attained in the future. Such an event would be a happy outcome of a variety of study which has been far removed from the realm of the practical.

IX. THE CLASSIFICATION OF CYCLOPIA.

Isidore Geoffrey St. Hilaire (121) was the first to show that monsters conform to some definite order and can be classified as Linnæus classified plants. According to his classification cyclopia belongs to the family of "cyclocephaliens" in the order of "monstres autosites," and has subdivisions according to the portion of the face involved, as ethmocephaly, cebocephaly, rhinocephaly, cyclocephaly, and stomocephaly. Gravelotte (31) modified this classification, making one general division of monstrosities to include arrests of development of the first cerebral vesicle, including typical cyclopia, atypical cyclopia and anophthalmia. Of typical cyclopia he described 5 degrees which are similar to the description of Bock already quoted.

Ballantyne (9) presented a logical classification slightly modified from Taruffi (123). His two chief divisions are monosomatous and polysomatous monsters. The latter include the various kinds of twins, triplets, etc. The monosomatous division is subdivided into pantosomatous, merosomatous, and heterotaxic. Cyclopia is a merosomatous monster and, in the language of the most common and generally accepted classification of "monstra in excessu" and "monstra in defectu," of course cyclopia comes in the latter division. Adami (1) and Stockard (115) feel that this simple division of monstrosities into two broad classes is convenient and sufficient. Of the monsters in defectu, Stockard (115) makes two subdivisions: (a) certain organs fail to complete themselves, as in cleft palate, hair lip, and faulty heart development; (b) certain paired organs occur singly or without mates, as in cyclopia.

Adami's Growing-Point Hypothesis.

Adami (1) has attempted to obviate the difficulties in classification by means of a single hypothesis, relating to the so-called

"growing points" of the embryo. Fischel has stated that the head and trunk centers are formed early in the embryo and that from these two centers the entire individual is derived. Adami discussed the method of growth in plants from two primary growing points, the superior giving rise to the stalk and appendanges, the inferior giving rise to the root, all parts being derived from these two. Mother cells give off daughter cells which persist as a vegetative layer; other cells given off at right angles to the former plane become functional cells of the stem and root. Secondary growing points occur. According to this explanation, Fischel's head and trunk centers are the superior and inferior growing points. These, once formed, do not grow but are projected apart. Successive daughter cells given off from these give origin to different segments of the body and their contained tissues, some daughter cells becoming secondary growing points for lateral organs. Assheton (4, 5) has demonstrated the superior and inferior growing points in the rabbit, frog, and chick. He found that the brain, medulla, heart, and foregut develop from the superior growing point, and all the rest of the body from the inferior. In animals the primary growing points cease to function as soon as the anlage or matrix of the main axis is laid down. Further increase in length is only by intercalation. If this were not the case there would be a mass of tissue with no function, as happens in epignathus and congenital sacral teratomas. These tumors are of epi-, meso-, and hypoblast, since they originate early in embryonic life before differentiation has occurred. Epignathus projects from the mouth, originating at the sella turcica where the superior growing point is located in the developed organism; congenital sacral teratoma is similarly located at the inferior growing point in the perineal region behind the rectum. Adami thus gives the first logical explanation of the location of so-called "fetal inclusions." His hypothesis is quoted freely here because of its general acceptability to teratologists, for whom it explains many difficulties, and because of its application to cyclopia in the light of Stockard's work. Adami would explain cyclopia as an abnormality of defect, being a "polar hypogenesis," "due to premature exhaustion of the growing point, or arrested growth of the same, at a period when the mother cells for the superior portion of the body and most of the head have been

given off. It is not that the lateral parts undergo fusion in the midline, having crowded out and arrested the growth of the more median superior regions; those regions have never developed, and the lateral parts have never been other than in apposition." Adami's hypothesis has the virtue of simplicity and it explains many questions of teratology which are not adequately accounted for by the various complex theories which have been advanced from time to time. Moreover, it has certain definite anatomic facts to substantiate it, the "growing points" having been localized in some animals. Stockard (118) does not accept it in detail, but acknowledges the value of its application to cyclopia where it accords with the facts of experiment. The "exhaustion of the growing point" is substantially the same conception as Stockard's "anæsthetic" action of magnesium salts and alcohol upon the fish embryo.

Cyclopia belongs, therefore, among the "monstra in defectu," being due to arrested development of the region of the superior growing point of the embryo, a "polar hypogenesis," as a result of which the optic tissues do not push lateralwards and become separated into two eyes.

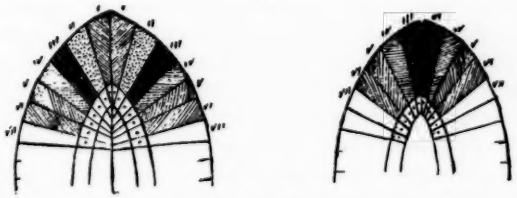

FIG. 4.—To illustrate Adami's "Growing-Point" Hypothesis as applied to cyclopia. 1. Represents the normal, the black portion (III) being the optic tissues after lateral extension. 2. Represents the cyclopean defect, the intervening median portions (I and II) being absent. (After Adami.)

X. PROBLEMS OF NORMAL EMBRYOLOGY.

1. *The Position of the Optic Anlage.*

The most important question in the embryology of the eye which has been clarified by the study of cyclopia is the question of the original position of the eye-forming material in the

primitive nervous system. Huschke (44), in 1832, stated that the eyes are primarily single and push out from a median position, separating into two eyes. He apparently did not distinguish sharply between the anlage of the eyes and the rest of the forebrain. Dareste (20) quoted Huschke without disapproval, but nearly every later writer on cyclopia has contradicted Huschke, sometimes with scant courtesy. In general his theory has been dismissed as not in accord with newer embryologic facts. On the supposition that the eyes are originally lateral, cyclopia has been regarded as a fusion of the eyes resulting from the absence of intervening tissues. Emphasis was thus laid upon the nonocular tissues. Experimental injury to the eye-forming material in the medullary plate at very early embryonic stages revealed that the eyes themselves are at fault and that cyclopia exists before the eyes separate from the brain. Spemann (105) was thus led to abandon the theory of fusion after this separation has taken place, and postulate a fusion within the medullary plate before the eyes have pushed out. In his latest papers he opposes Stockard's conclusion that the eye is originally median, though his own experiments seem consistent with this conclusion. Stockard (118) and Mall (64) have both confessed their inability to follow Spemann's reasoning. Lewis's (59) experiment of removing median tissue with a needle and getting cyclopean eyes would favor the theory of a fusion brought about by the absence of intervening non-ocular tissue. Stockard (115) suggests, however, that ocular tissue may have been injured in these experiments. A strong argument against the theory that non-ocular tissue is primarily at fault allowing the eyes to fuse, is the fact that the cyclopean eye is smaller than two normal eyes. If the eyes are not at fault originally they should equal the sum of two eyes when fused. Stockard has proved that the cyclopean condition is present at the earliest stage at which it can possibly be recognized; that there is no evidence that eyes which have once been separate have fused later; that cyclopia exists when the eyes are still closely attached to the brain; that the cyclopean eye comes off from the brain in its final condition.

So convincing was the accumulated evidence in favor of the median position of the anlage that Stockard (118) carried out a series of experiments on the salamander *Amblystoma*

punctatum, cutting out portions of the medullary plate to determine just what part of this plate is essential to the production of eyes. After removing lateral portions of the medullary plate in thirty embryos he found that twenty-four developed both eyes while six showed absence of one eye. In only one of these were both eyes absent; in this case the cut was more median than was intended. Nine embryos had a narrow median strip removed from the anterior portion of the medullary plate. Four showed entire absence of the eyes. In four others the eyes were highly defective. In one embryo the eyes approached a normal condition; in this case the strip of tissue removed was exceedingly narrow. It is to be noted that the removal of a median strip should produce cyclopia, according to the theory that this deformity is due to the absence of tissue between the anlagen of laterally placed eyes; but cyclopia did not occur. Stockard concludes: "the eye anlage in the medullary plate occupies an antero-median position as shown by the various abnormalities incurred when this region is cut away. The failure to injure the development of the eyes in the great majority of cases where the lateral portions of the medullary plate are removed by operation indicates further that the eye anlagen do not occupy lateral positions during this stage of development." Stockard discusses, further, the necessary development of the optic stalks on the assumption that the eyes are originally lateral. As the walls of the neural tube mount up and brain tissue comes to lie below the original lateral aspect of the medullary plate, the optic stalks would necessarily be within the brain and not below it, a condition which never occurs. The evolution of the neural tube, leaving the optic nerves and chiasm below and outside the brain, is only possible if the eye-forming material is originally median, occupying a position in the medullary plate which is not disturbed by the development of the lateral tissues as they grow upwards.

Thus, the logic of the situation and experimental facts support Stockard's belief that the tissue from which the eyes develop is originally in the midline of the medullary plate at its anterior end. Mall (64), in his last contribution, states that Lewis told him that only a few cells separate the eye anlagen in the midline. The difference between Lewis and Stockard,

after all, is a question of the most minute histology of the early embryo, and whether we shall speak of the "anlagen" sepa-

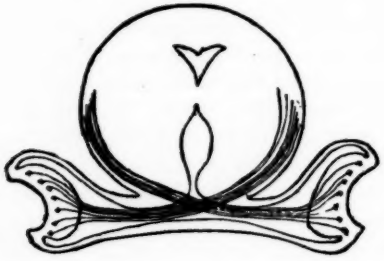

FIG. 5.—A diagrammatic cross section through the brain and optic cups of an early embryo, with all of the median ventral medullary tissue represented as being part of the optic stalks. The future fibers of the optic nerves follow the optic stalks to the median plane where they cross and afterward enter the brain to pursue their course as the optic tracts. The optic cross is entirely beneath and outside the brain. (After Stockard.)

FIG. 6.—A sketch representing the actual outlines of a cross section through the brain and eyes of a late fish embryo. The optic nerves cross below and outside the brain and are surrounded by cells derived from the original optic stalks. (After Stockard.)

rated by a few cells or the "anlage" of the eyes, the fact seems clearly established that the eyes originate from a primordium median in position in the medullary plate and not lateral.

This fact is exceedingly important for the understanding of cyclopia and of the normal infracerebral position of the optic nerves and chiasm in the mature state.

It is to be observed in all deductions from experimental work that precisely the same conditions cannot be postulated for widely differing species. All human embryology suffers from this element of uncertainty because our knowledge is based largely upon the study of lower forms of life. It may

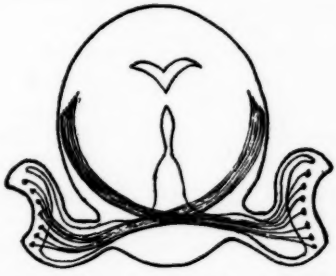

FIG. 7.—A diagrammatic cross section through the brain and optic cups in an imaginary case in which the optic connections are lateral with median brain tissue originally lying between the eye anlagen. The future optic fibers growing along the optic stalks as paths reach the lateral points on the brain from which the stalks arose and then enter the brain tissue before having formed the cross. Continuing to grow, the optic nerves meet and cross in the median plane. The cross is within the brain itself and lies above the median mass of tissue which has always existed between the eyes. No vertebrate brain exhibits such a condition. (After Stockard.)

fairly be said, however, that in the early stages of embryonic life there is a practical identity in the various species, and the criticism to which much of animal experimentation is liable does not apply to deductions from embryologic study. However widely adult human eyes may differ from those of fishes, the early embryonic status of the neural tube and the anlagen of organs developing from its anterior extremity must be practically identical throughout the vertebrate realm.

2. *The Origin of the Optic Nerve.*

It is no doubt generally believed that the optic nerve is derived from the ganglion cells of the retina. This is a logical

conception in accord with the facts of neurologic anatomy, viewing the optic nerve as a sensory nerve transmitting impulses to the brain, or as a cerebral tract (which is more correct), representing a sensory neurone of the third order. There is not, however, a unanimous opinion in the literature. As late as 1904, Mayou (66) described the retina and optic nerve of an ancephalous specimen and concluded, from the faulty development of the nerve fiber and ganglion cell layers of an otherwise normal retina, that the axis cylinders constituting the optic nerve are derived from cells of the primary optic centers and not from the retina. The older anatomists apparently held the same opinion. Jaboulay (45) reviewed the subject in 1886 and referred to the quadrigeminal bodies as the source of the optic nerves in the writings of Morgagni, Winslow, Zinn, Gall, Magendi, and Meckel; the quadrigeminal and geniculate bodies, in the opinion of Sappey and Huguenin. Marshall and Kolliker thought that the nerves are centrifugal. Some of the textbooks merely state that the optic stalks give rise to the nerves.

Jaboulay (45), in his important monograph, called attention to the value of cases of anencephaly on the one hand, and of microphthalmos with normal brain on the other hand, in clarifying the subject. He quoted Pierrot's conclusion that the optic nerves have a certain autonomy as exhibited in anencephaly with intact optic nerves. Jaboulay found that normal optic nerves did not occur with microphthalmos and anophthalmos, though a normal brain existed. He concluded that the retina exerts a trophic influence upon the nerve. Oakden (85) studied two anencephalous fetuses, using normal eyes of fetuses of the same age as controls. He found no wide departure from the normal; the nerve fiber layer of the retina was thinner in the brainless cases and the ganglion cells were fewer. Manz (65) stated that the eye in anencephaly differs from the normal only in the absence of nerve fibers from the optic nerve and retina. Vaschide and Vurpas (126) found a normal retina in an anencephalic cyclopean monster. The careful staining methods used by these authors make their observation valuable. Lewis (57) transplanted the optic vesicles of amblystoma into an abnormal location in the same embryo and into older embryos and found that optic nerve fibers developed. Similar

experiments on rana palustris gave the same result. Stockard (117) found that abnormal eyes of fundulus, disconnected from the brain, grew nerve fibers which passed through the pupil, taking the path of least resistance according to Stockard's suggestion.

Following the well-known investigations of Cajal, authors have very generally accepted the retinal origin of the greater portion of the fibers which constitute the optic nerves. The standard textbooks state that these nerves are centripetal, originating from the ganglion cells. The more elaborate statements refer to smaller numbers of centrifugal fibers in addition to the preponderant visual fibers which are centripetal. Thus, Piersol says that there are (1) fibers going towards the retina, originating in the brain from cells of the primary optic centers or from sympathetic neurones, which probably carry vasomotor impulses to the retinal blood vessels; and (2) perhaps fibers by way of a center in the medulla pass from the retina and may convey indirectly to the third nerve nucleus the impulses resulting in pupillary movements.

The observations upon anencephalic specimens are extremely variable. Unquestionably some of the lower vertebrates can develop a perfect optic nerve in the absence of a brain. There is, in other words, an autonomy possessed by the retina. In higher forms it is scarcely possible that the embryonic nervous system can be so profoundly altered within very narrow limits that certain parts are destroyed while adjacent parts escape entirely. It is not reasonable to expect a perfectly normal retina in anencephaly. It is much more probable that the nerve fiber and ganglion cell layers of the retina share in a widespread damage to the nervous system than that they fail because the primary optic centers are absent. With this conception in mind, one is not surprised at the variable case reports in the literature. The retinal damage may be very little or very great. Where there is but little diminution in the size of the nerve trunk and the nerve fiber layer of the retina it may be possible that the centrifugal fibers alone are absent as a result of failure of the brain tissues which give origin to these fibers.

The evidence obtained from the study of poorly developed eyes with normal brains, and of well-developed eyes accom-

panied by extensive brain defects, points to the dependence of the optic nerves upon the retina rather than the brain. Eyes with grave developmental defects do not have well-developed optic nerves, however normal the brain may be; eyes which approach the normal, even with the defects inherent in cyclopia, often show a partial development of the optic nerves which occasionally approximates the normal. While it cannot be claimed that conclusive proof of the retinal origin of the optic nerves is obtained from a study of monstrous eyes, it may be stated that the evidence is consistent with the logical belief that these nerves, in so far as their preponderant visual fibers are concerned, are the outgrowth of the ganglion cells of the retina.

3. *Self-Differentiation of the Crystalline Lens.*

The crystalline lens is a peculiar structure in many respects. Apparently it has not always had an intimate relationship with the eye, but was once an independent organ, perhaps sensory or designed to focus light upon the brain wall before the eye was evolved as a separate visual organ. Originating outside the optic cup and eventually coming to occupy an intra-ocular position, its dependence upon the influence of a surface ectoderm and an optic cup seems evident. The old idea that the lens pushes the optic vesicle before it making an optic cup scarcely needs mention as it is generally discredited. Lewis (58) expressed what is perhaps the most generally accepted view when he said that "the lens is neither self-originating nor self-determining, but is dependent for its origin, its size, its differentiation, and its growth on the influence of the eye." He found that in rana sylvatica the optic cup gave rise to a lens from its own tissues if prevented from stimulating a lens from the ectoderm of the body wall. In rana palustris, on the contrary, optic cups failing to come in contact with the ectoderm did not form lenses. Stockard (116) did not find lenses when the optic cups were deeply buried away from the ectoderm, in fundulus. There is evidently a difference in various species in the ability of the optic cup to develop a lens from its own tissues. The well-known tendency of salamanders to form a new lens when the old one is removed or pushed back into the

vitreous, or the iris injured, is not shared by most animals. Applying his theory of dependent lens formation to cyclopia, Herbst (36) said that "if the lens really developed independently of the optic cup then in the case of median cyclopia the two lateral lenses should arise in their usual positions; but they do not, and furthermore the cyclopean cup gets a lens from ectoderm out of the usual lens-forming region." Spemann and Mencl (69, 70, 71) have discussed the problem of the crystalline lens in numerous valuable contributions.

Spemann (101) and Lewis (56) concluded that no localization of lens-forming material occurs in any given area of ectoderm, but that lens formation is due to stimulation of ectoderm through contact with the optic vesicle or cup (in amphibians). Spemann (106) found later (1912) that several varieties of frog produced lenses independently of an optic cup, and suggested that King's (49) experimental animals might have shown lenses if they had been allowed to live longer. King had concluded that the lens, in rana esculenta, was entirely dependent upon the optic cup. Stockard (115, 116), however, showed in fundulus that lenses occurred without a trace of an eye, that lenses occasionally appeared in the usual lateral position when the eye was median; and one of his specimens was an incomplete diprosopus with three eyes and one additional lens. He also found that the size and shape of the lens were often out of accord with that of the optic cup; the smallest trace of an optic cuplike structure sufficed to develop a lens if in contact with the surface ectoderm, though this ectoderm was far removed from the usual lens-forming area. Stockard concluded from these observations that the lens may be self-differentiating but that the optic cup exerts a much stronger influence for the production of a lens than the innate tendency of the ectoderm to produce an independent lens. Therefore, he believes that the injury done to the ectoderm in removing the optic vesicles by experimental methods may be sufficient to destroy the limited capacity of the ectoderm to form a lens; he would not conclude from such experiments that the ectoderm, uninjured, has no power to produce a lens when the optic vesicle is removed. Stockard (118) found the separate lenses in cyclopean fishes to be anterior to the eye most often. The lens-forming power would seem to diminish from the anterior tip of the

head, backward. The trunk ectoderm did not give rise to lenses. Spemann (106) likewise failed to get lenses from the back ectoderm of frogs by transplanting the optic anlage to this location.

Stockard's conservative statement, based on the large material observed, may be accepted as a fair conclusion. The crystalline lens possesses a certain degree of independence, perhaps a relic of its original separate existence. It is most often, however, found in intimate relation to an optic cup whose power to stimulate lens growth in overlying head ectoderm is much greater than the tendency of the ectoderm to grow a separate lens.

XI. CONCLUSIONS.

Cyclopia is a monstrosity of the type known as "monstra in defectu," being the result of a failure in development of the anterior end of the embryonic nervous system. According to Adami, this may be considered a superior polar hypogenesis affecting the region of the superior growing point of the embryo.

Cyclopia is not a germinal defect, but is a developmental defect resulting from some detrimental influence acting upon the embryo after cell division has begun. The damaging agent seems to act by exerting an inhibitory or anesthetic effect upon the embryonic nervous tissue.

Dareste's widely accepted theory that cyclopia is the result of a premature closure of the anterior orifice of the neural tube has been abundantly disproven. Amniotic bands as a cause of cyclopia are, in the words of Mall, a myth of teratology.

In lower forms of life the cyclopean defect may be sharply delimited, but in man and the higher vertebrates it is part of an extensive defect of the nervous system which may appropriately be termed cyclopcephaly.

Cyclopia is not the result of a failure of intervening non-ocular tissue to develop, allowing two lateral eyes to come together. It is the result of damage to the eye-forming material in the medullary plate, by which separation and lateral extension of the eyes is prevented. The failure of non-ocular tissue to develop is the result and not the cause of cyclopia.

The study of monstrosities and pathologic ova offers hope that these calamities can be prevented if pathologic uterine conditions and substances in the maternal circulation which are toxic to the embryo are removed.

The study of cyclopean eyes and experiments suggested by this study indicate that the eye-forming material is median and not lateral in the anterior portion of the medullary plate of the embryonic nervous system. Practically, a single optic anlage exists, from which two eyes develop by lateral outpushings. Whether a few cells in the midline intervene between the two halves of this anlage, according to Lewis, or no such separation exists, according to Stockard, is a question of little practical importance.

The logical opinion that the optic nerves originate from the ganglion cells of the retina rather than from cells of the brain is strengthened by the study of cyclopean specimens in which the brain is absent or rudimentary.

The study of cyclopean eyes in lower vertebrates indicates a degree of independence on the part of lens-producing ectoderm of the head end of the embryo. This self-differentiation of the crystalline lens is, however, a much less potent factor than the influence of the optic vesicle upon lens production.

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PERIMETRIC METHODS.

A Discussion at Oxford Ophthalmological Congress, July, 1920.

By Dr. P. G. DOYNE.

DR. LUTHER C. PETER (Philadelphia) contributed the opening paper. The laboratory and the consulting room are distinct entities, methods which are employed in the one are not necessarily applicable in the other. For the consulting room the method must be practical, easy of application, and reasonably speedy. With advancing knowledge the mere silhouette of the field is not sufficient and it is necessary to use methods which accurately delineate the changes peculiar to the central zone. The tangent plane is now the instrument of choice in all central field studies. It is admitted that an error may creep into the findings between the 20 and 40 degrees areas if a movable stimulus is employed this error is so small as to be negligible. One of the most marked advancements made in the tangent plane is its use in certain studies at close range. The Peter hand campimeter—in this instrument the average normal blind spot of Mariette is placed and outlined on the screen and it is advised that the study should begin by the outlining of the normal blind spot; the advantage of this procedure lies in the recognition of unsuspected cases of enlargement and in the training in concentration which the patient receives. Gradle's laboratory screen—this instrument is operated at a distance of sixty centimeters and a second point of fixation is interposed midway between the patient's eye and the fixation point on the board. The average normal blind spot is marked out and the test objects consist of metal balls of definite sizes which are moved by a magnet from behind the

screen. This instrument is, however, too technical for ordinary practice.

The Bjerrum method of study at one meter radius is most suitable for examining small scotomata which elude accurate study at close range. Lloyd's stereo-campimetric slate—this is an admirable instrument, accurate and expeditious. Elliot's Scotometer—this is in many ways a practical instrument, but is liable to error if not used with extreme care. The fact that the movement is circumferential only makes for inelasticity and there is a tendency for the production of sharp angles. The screen is excellent but the test objects might with advantage be larger.

Though the circumferential movement is preferable to the radial, yet the outstanding advantage of the tangent scale is the freedom of the movement obtained by using a hand-manipulated test object.

Regarding the distance of the eye from the test object; there is, in favor of the short range, the sharper definition of the test object, the prompter recognition of color tones, and the ease of concentration on the point of fixation. It is of course essential for the patient to wear his correction for ammetropia or presbyopia, should any exist.

At the longer range, one meter and upwards, the differences between the central and peripheral zones are more pronounced; to compensate for this it is advised that a slight movement be imparted to the test object when exploring the peripheral zone. When working at one meter—and longer distances are not advised—there is no doubt that greater accuracy can be obtained in marking out small scotomata, provided that the test object used subtends the same angle as subtended by the test object employed on the smaller scale. Considering the test object; it is desirable, in view of the number of perimeters and screens with differing radii in use, that the object should be named by reference to the angle which it subtends at the eye, rather than by its linear measurement. The tendency has been to use too small a test object. For central zone work the test object should subtend an angle of one half a degree, and for the peripheral zone an angle of two degrees. This should suffice for colors also. It has been shown by many workers that a big drop in visual acuity occurs in the zone immediately outside

the fovea, particularly in regard to color sense; consequently it is unsatisfactory to use the same stimulus for the two regions.

Regarding the exposure of the test object to the eye, it is desirable to pass the object from invisible to visible areas and when testing the periphery to impart a slight vibratory movement to it.

The following are the probable important changes which will be incorporated in future methods:

1. Perimetry will be largely practiced on the tangent scale.
2. Light standardization; (the "Daylite" lamp unit is advised).
3. The central and peripheral field will be studied by a stimulus moved by hand.
4. Pre-exposure and the surrounding field will be equal in brightness to the stimulus employed.
5. Determination of the threshold values of different parts of the retina in health and disease by means of light standardization, with photometric measurements made possible.

The central vision is absent in one eye, but the muscle balance is good, Lloyd's stereo-campimetric slate is the instrument of choice; but when one eye is totally blind, squint or muscle imbalance is present, or when both maculæ are involved, field taking requires special technique. The following method is suggested. The patient is seated at the perimeter, with the arm of the instrument in the horizontal plane. He is told to look along the arm until the fixation spot becomes visible, the number of degrees that the eye has been rotated is found by taking the corneal reflex as in a squint. This process is repeated in the four cardinal directions of the eye. The four points, so determined, mark the border of the central scotoma. They can be placed on the screen and used for fixation and the rest of the field studied.

E. MARX (Leyden): The ideal method for performing scotometry is one in which all extraneous stimuli are excluded as far as possible. The following method is brought forward as one in which only the essential stimuli are placed before the patient and one which is easy and practical in its use and application. A large black cloth 4 ft. by 6 ft., of dull woollen material is used as a screen. The fixation point is attached at a height of 4 ft. 4 in. from the ground; on the side of the screen

away from the patient circles and radii are marked out; the patient is seated one meter from the screen. Eight or ten small holes, a few millimeters in diameter, are made in the cloth at the height of the observer's eyes, through which he can see the patient. The test objects are small steel balls of varying diameter which the observer manipulates from behind the screen by means of a hand-magnet, marking on the back of the screen the outline of the scotoma.

In cases where there is a central scotoma, it is necessary to enlarge the fixation point to a more or less extensive fixation field. It is better to have a white ring surrounding a black center than to merely enlarge the usual white fixation point, as tests can be made inside the ring. Experience points to the fact that persons with central scotomata can keep their gaze fixed in the center of a white ring, the size of which varying with the size of the scotoma.

By observations on the artificially produced scotoma of the dark-adapted eye in normal persons, this factor was proved.

The subject, having been for a certain time in a dark room, was placed before a ring covered with luminous paint. In the center of the ring there was an instantaneous shutter and behind the shutter a Nernst lamp with a vertical filament. As the subject is attempting to fix the center of the ring, the shutter is opened for a fraction of a second; a sharp afterimage is thus produced which the subject then draws on a previously prepared paper with a dark fixation point. By this means it is possible to find out how far outside the center of the luminous ring the eye has fixed. The error has never been found greater than one degree fifteen seconds in any direction.

Professor Van der Hoeve (Leyden): It is necessary to make our methods as good as possible for quick examination. Hasty perimetry is worse than useless, yet with our present instruments there is often not time for their systematic use in the clinic.

There is a tendency for the size of the test object employed to be too small. The only rational method of outlining a scotoma is to approach its boundaries perpendicularly with the test object, but the presence of the scotoma must be first elicited. The following is a good method to employ: Carefully map out the blind spot; encircle this in two or three circles, the first

circle very close to it, the others at some distance from it, then ramble with vertical movements all over the region from fifteen degrees on either side of the fixation point and the same distance vertically.

He agreed that Seidel's sign was very important in the early diagnosis of glaucoma, but often the earliest scotoma appeared at the median raphe and Bjerrum's arcuate scotoma might be complete except for the area immediately adjoining the blind spot—a negative Seidel's sign. Bjerrum's scotoma hardly ever began all at once, usually scotomatous islets appear along the course of the bow, eventually joining up. The scotoma might be absolute or relative in part or in whole.

He protested against the view that a bridge was present between the scotoma and the blind spot in every case of scotoma caused by disease of the optic nerve.

Dr. Sinclair (Edinburgh). He was disposed to say that the perimeter should not be ruthlessly cast aside. It was usually badly made. The test object should be moved by hand and the use of the instrument should be limited to the mapping out of absolute scotomata and the limits of the visual field. He urged the importance of the small test object for white, for colors a larger test object was necessary. With regard to the screen he preferred the two-meter screen for delicate work. The screen was of value for central zone work, but not for the periphery. It was especially valuable for detecting early relative defects in the central zone. He advocated moving the test object from blind to seeing areas and vice-versa. He emphasized the importance to general medicine of the findings of these tests.

Professor Harvey Cushing (who was asked by the Master to join in the discussion). After some introductory remarks he pointed out that all were striving to produce instruments of precision. Not so very long ago a similar discussion was taking place among physicians regarding different kinds of thermometers. The introduction of these instruments meant the taking of more and more time in the clinical examination of the patient. It was necessary also that an instrument should be produced which was more or less fool-proof. Changes in the periphery of the field were at present of most direct importance to brain surgeons. He would mention the temporal lobe. He

would point out how far forward the visual pathway went in the temporal lobe, so that any lesion in this lobe would be likely to produce an homonymous defect in the fields. Curiously that defect always came first on the same side as the lesion, and it might advance as far as a quadrangular defect before any defect appeared in the opposite field at all. In the case of temporal lobe tumors one could tell by bilateral changes in the field whether the tumor was high or low because these paths showed the same kind of course through the brain.

It was necessary that there should be some form of field taking applicable to all patients and which could be used whether the patient was sitting up or in bed. He hoped that as the result of this discussion something would be evolved which could be passed on to those who, while not being specialists, were interested in ophthalmology.

Dr. S. Holth (Christiania): In testing the peripheral fields, the object must not be moved too slowly for then it may not be observed, though no actual scotoma is present; conversely if moved too fast a scotoma may be missed. In testing the periphery of the field the perimeter is indispensable, the ordinary models, however, are too cumbersome, especially for travel and the sick-bed.

The Holth Chord Perimeter.—This instrument meets these requirements and in addition there are superadded to the instrument a sensitive test for central scotoma and a centimeter-diopter measure.

The instrument consists of two rules, 27.5 *cm* long, connected at a right angle by a joint which forms the fixation point. The chord graduation occupies 25 *cm*. Two metal sticks, attached to the rules, when at right angles have their connecting point in the center of the half circle. The test object is moved by hand along the rules.

On the outer side of the rules, groups of three celluloid disks, in pink, red, and white, are placed. The patient fixes the middle disk of the three and the rule is held first in the horizontal and then in the vertical position. A comparison of the relative light and color values of the three disks can then be made.

The two chords can be straightened and fixed and so converted into a centimeter-diopter measure.

Mr. E. H. E. Stack (Bristol) emphasized the importance of

having a moving disk instead of a fixed one for ordinary perimetry and of the necessity of working from blind to seeing areas as well as in the opposite direction. He advised routine 4 or 5 point perimetry to be performed by the sister or assistant in the clinic. By this routine procedure unsuspected cases, needing detailed perimetry, were often discovered.

LIEUT.-COLONEL ELLIOT (London) wished to confine his remarks to glaucoma. He had evolved his present scotometer while studying Seidel's sign. Scotometry was of value in glaucoma in three ways:

1. Diagnosis in early cases.
2. Following the progress of a case.
3. In the estimating the value of treatment.

He maintained that his instrument, while not necessarily a laboratory instrument, was a practical instrument for clinical purposes. By 26 rapid and precise observations the field could be accurately delineated out to the 26 degree circle. He wished to insist on the importance of accurate fixation of the head so that the eye remained in the center of the system of circles under examination. He regarded Bjerrum's principle of enlargement of the scotoma as of the greatest importance. It seemed to him unreasonable to expect that the enlarged blind spot should always end in pointed extremities. It was more reasonable to suppose that the resulting scotoma would be frayed out into a number of points, owing to the fact that certain nerve bundles would be more damaged than others as they flowed over the scleral edge. The advantage of the circumferential method consists in the fact that one was following the path of the damaged fibers, as the path of these fibers is a circular one around the center of the retina.

With regard to the forms of the scotomata, one might find:

1. An enlarged blind spot with jagged edges above and below.
2. A single narrow arc-like belt continued along one or two degree circles only.
3. No enlargement of the blind spot but at some distant point a commencing relative or absolute scotoma.

Other varieties also could be found. The reason for these peculiarities lay:

1. The method of distribution of the nerve fiber bundles as they pass out of the papilla.

2. In ill-understood physical variations of the scleral edge causing a patchy lesion of the nerve fibers.

With his scotometer the observer can pass the test object from visible to invisible areas and vice versa. The scotoma would be most exaggerated if the test object was passed from invisible to visible areas.

DR. A. MAITLAND RAMSAY (Glasgow) called attention to the value of the spindle-shaped enlargement of the blind spot in sympathetic irritation. The value of the observation depended on the fact that after the exciting eye had been removed the blind spot resumed its normal shape. He placed great value on this sign in enabling him to determine when it was necessary to excise the exciting eye. He had found DR. PETERS' campimeter most useful in accurately and quickly making this observation.

MAJOR LISTER, I. M. S. (Lucknow) pointed out the value of a series of observations of the blind spot in estimating the progress of a case of glaucoma. Though modern instruments for scotometry were desirable they were not always obtainable, but it was possible by means of extemporized methods to take sufficiently accurate observations. He cited the case of a gentleman with glaucoma, who was filling a very important post in India. In this case, for reasons of state, it was most desirable to postpone operation, and by watching the size of the blind spot, using extemporized methods—a black billiard cloth and a piece of chalk—it was possible to watch the progress of the case with confidence.

MR. T. HARRISON BUTLER (Leamington) in using the ordinary Bjerrum's screen he measured the distances from the center with a Sinclair's tangent scale. He used a carpenter's rule to measure the angular distances. The best varieties of these have a scale of degrees at the pivot and by opening the scale one can apply it to the screen and transfer the reading to a chart.

MR. E. BURDON-COOPER (Bath) put forward his method of measuring the blind spot "longitudinally." Of two spots on a card one looked at the central one with one eye in such a way that the other spot fell on the blind spot of the eye. By ap-

proximating or receding the chart on a longitudinal bar two points could be found where the spot just appeared or disappeared. The longitudinal distance between these two points was a measure of the blind spot. In thirty seconds an accurate measurement of the blind spot in one diameter could be made.

Mr. E. E. Maddox (Bournemouth). It was necessary to have a rapid method for singling out cases for more detailed perimetric study. He used a white hatpin stuck into a cork for this purpose. Owing to the cylindrical shape of the cork, it can be held between the thumb and forefinger and a movement imparted to it without any chance of the movement of the fingers being seen. He considered it desirable to impart movement to the test object when examining the peripheral field.

Mr. P. G. Doyne (London) said that during the last few months he had made some observations on the blind spot in myopia, using sometimes Elliot's scotometer, sometimes Bjerrum's screen. The object which he had in view was to see if the enlargements of the blind spot, so common in myopia, might be a source of confusion in the estimation of the value of Seidel's sign. He had not yet taken sufficient observations to draw definite conclusions, but in some cases of myopia, in which there was no reason to suspect glaucoma, appearances very similar to Seidel's sign were obtained.

There appeared also to be no reliability in the estimation of the condition of the retina which overlay areas of atrophy or stretching, so common around the myopic disk. He had lately examined a case in which there was a large inferior crescent, about two papilla-diameters in extent, and yet no enlargement of the blind spot was found.

REPORT OF THE PROCEEDINGS OF THE SECTION ON OPHTHALMOLOGY OF THE NEW YORK ACADEMY OF MEDICINE

By Dr. CONRAD BERENS, Jr., Secretary

MEETING OF OCTOBER 18, 1920. DR. A. E. DAVIS, CHAIRMAN.

Doctor Martin Cohen and Doctor Ward MacNeal read a report of a case of **metastasis of carcinoma into an endothelioma of the optic nerve sheath** (complete report to appear in next issue).

Doctor A. E. Davis and Doctor H. V. Hubbard gave a report of two cases of **Coats's disease.**

Case 1.—Aged ten. Came to the clinic at the Post-Graduate Hospital September 18, 1920. Family history negative. The right eye was found defective in December, 1919. V. O. D. $\frac{1}{10}$ eccentric.

In the right fundus there is a large mass of white exudate, yellowish in some spots, under the retina, extending from the temporal half of the optic disk, upon which it encroaches, to the extreme temporal periphery of the fundus. The highest point of this mass measures + 8 about one disk-width to the temporal side of the disk. At this point some blood vessels extend from the mass into the vitreous. There are numerous hemorrhages on the surface of the mass near the macula, especially beyond the macula on the temporal side. Some of the vessels are dilated into a fusiform shape, as described by Coats. Numerous cholesterin crystals are scattered throughout the mass, especially at the margins of the exudate. One of the unusual features in this case is that one of the retinal vessels is veiled for a short distance in the lower portion of the

mass. The vitreous and anterior portions of the eye are clear. T. n. The other eye is normal.

The subcutaneous tuberculin test was positive in all three phases, the changes in the eye-ground consisting in fresh hemorrhages.

This case belongs to the second group reported by Coats, with the massive exudation into the retina with marked vascular changes.

There is one feature in this case which has not been observed before, that is, the absence of the light streak on the retinal vessels over the massive exudate, or, if present, the streak is but very faintly to be seen. This corresponds to cases of ordinary marked detachment of the retina where no light streak is seen upon the retinal vessels; and, incidently, it goes to confirm the theory that the light streak produced on the retinal vessels is due to refraction and not to reflection, a point that both Loring and myself contended for many years ago and in which I confirmed the experiments of Loring.

Another feature unusual in these cases of Coats's disease is veiling of one of the retinal vessels in the lower part of the mass, as in this case. Coats claims that this is a very rare condition.

The cause of the trouble still remains obscure. By many observers it is considered to be due to tuberculosis. Coats, however, was not inclined to this view and thought it due wholly to hemorrhages into the deeper layers of the retina. But as to the causes of the hemorrhages themselves he was not certain, and that, of course, is the point in the whole discussion.

DISCUSSION: DOCTOR MARTIN COHEN said the obliteration of the retinal light reflex in the artery as it coursed over the massive exudate was probably due to an obliterating endarteritis or a localized exudate. The massive exudate was evidently not due to a previous hemorrhage, as there were only a few hemorrhages seen in the periphery of the fundus, but none in the mass or its vicinity.

DOCTOR L. W. CRIGLER said that he had reported a similar case before the section in which he was fortunate enough to secure the eye for microscopic examination inasmuch as it became necessary to remove it on account of secondary glaucoma. His case differed materially from those described by

Coats in that there was very slight deposition of connective tissue beneath the retina. There was a progressive atrophy of the inner layers of the choroid and the outer layers of the retina. A coagulum filled the space between the retina and choroid in which there were deposits of cholesterin and clouds of "ghost cells." In every other respect, the case presented the identical changes described by Coats, classified under Group II.

Doctor Davis in closing said that the loss of the light streak in the patient was not due to endarteritis obliterans for the vessels were full of blood.

DOCTOR K. SCHLIVEK presented a patient with **persistent hyaloid arteries.**

F. L., 9 years old, was sent from school on account of imperfect vision.

Vision $\frac{1}{2}\frac{5}{0}$ each eye—with correction $\frac{1}{1}\frac{5}{5}$.

O. D. There is a persistent hyaloid artery. It begins at the optic nerve, comes forward and close to the lens divides into three branches which subdivide dichotomously into several minute ones. They can be traced beyond the limits of the lens.

O. S. Almost the same condition but there are only two branches which subdivide and one small single branch.

Persistent hyaloid artery is not a very rare condition but the picture presented by this patient is unusual. The hyaloid artery generally is single; it begins at the optic stem and goes forward to the posterior pole of the lens. Here it divides into numerous branches which spread over the posterior surface. It also has some branches which supply the vitreous. There are several variations. Occasionally it may divide into two branches soon after leaving the optic stalk and rarely, as in this case, it may divide into three or four branches when nearer the lens.

DISCUSSION: DOCTOR CLAIBORNE said that he had reviewed the literature of this subject a number of years ago, and that his paper could be found in the Transactions of the Section. He said that the cases in which the arteries plunged forward into the vitreous humor towards the lens returning upon themselves and then into the optic nerve head, had been classified with the remains of hyaloid arteries. He thought this was an improper classification.

DOCTOR GEORGE H. BELL presented a patient with **Parinaud's conjunctivitis** in a physician, age 30, with marked swelling of both upper and lower lids; the conjunctiva was highly inflamed and the characteristic lesions were present consisting in large reddish polypoid vegetations. There was a mucopurulent discharge and also enlargement of the pre-auricular glands. The temperature was 101°. The condition for a time seemed to get worse with more swelling of the eye-lids and more glandular involvement. Ten days later, the pre-auricular gland was so swollen that it was opened and drained. The patient's temperature then ran up to 104° and continued high for three days. The parotid and sub-maxillary glands became more involved and very much swollen. The smear and culture from the conjunctiva showed only one variety of white staphylococci. The patient had no pain, and there was no involvement of the other eye.

The usual treatment for septic conjunctivitis was instituted and now after five weeks the edema of lids and conjunctiva has about disappeared. The granulations in the conjunctiva are gradually absorbing and the glands are all receding.

DISCUSSION: DOCTOR WOLFF said that a few months ago he had treated the five-year old son of a physician who showed marked granular swelling in the fornices and tarsal conjunctiva of both lids of the left eye. There were numerous ulcerated areas covered by a grayish exudate. The pre-auricular gland of that side was very much enlarged. The case was clearly one of Parinaud's disease. Pathological examination, inoculations into the peritoneum of a guinea pig and the anterior chamber of a rabbit's eye showed the case to be tuberculosis. After treatment for two months with x-rays, dusting with iodoform and frequent irrigations, the case was entirely cured.

DOCTOR C. E. MCDANNALD in describing an **instrument devised for the removal of cataractous lenses in their capsules** said: In studying the method and instrument used by Dr. Barraquer for the performance of the operation designated by him as phakoerisis it occurred to me that a much simpler device could be substituted. With this thought in mind I visited a jeweler, and laid before him Dr. Barraquer's article with my suggestions as to the modification of the instrument shown in

the half-tone cuts that were employed to illustrate his technique. I concluded to have made a suction tip resembling, as near as possible, the one employed by him in his demonstrations. This was accomplished by drawing down a silver tube until its smallest outside diameter equalled one and one half *mm.* It was then bent at an angle of about ten degrees, the end flared out and a suction cup fashioned two and one half by three *mm* and one half *mm* in depth. The tip which was four and one half *cm* long was then soldered in the end of a larger tube nine *cm* long. Six and one half *cm* from the end of the suction tip a four *mm* opening was made in the large tube. This hole was situated where the index finger could easily be slipped over it for the purpose of making and breaking the suction, in this way eliminating the valvular mechanism spoken of by Dr. Barraquer as being necessary for the proper manipulation of his instrument in applying and discontinuing suction. The metal tube was then inserted in the open end of a rubber connection tube which was attached to a number fifty Sorensen rarefication pump. I found that the finger when placed over the opening indicated for this purpose acted perfectly as a valve, thereby enabling me to control my suction at will without stopping the pump. I determined to try this instrument on the first docile patient I had for cataract operation. The case selected was one with a mature senile cataract and well sclerosed lens. The technique was the same as that which I have hitherto employed in combined extractions, namely a corneal section with conjunctival flap and iridectomy. The instrument was then introduced into the anterior chamber and placed in contact with the lens a little above the equator. The capsule was instantly picked up by the suction cup when the finger was slipped over the opening in the handle of the instrument. By means of a side to side and forward and back movement the lens was loosened in the patella fossa. The instrument was then lifted slightly forward, which elevated the corneal flap thereby allowing the brim of the lens to emerge from underneath the scleral border. After this it was easily withdrawn. The patient made an uneventful recovery with little or no reaction from the operation.

This is submitted purely as a preliminary report and will be

followed later by a full account of the cases that I have treated by this method.

DISCUSSION: DOCTOR PAGANELLI said that he had seen Doctor McDannald's first operation and had also extracted a cataract using his instrument. He easily extracted the lens, although his section was small and had to be enlarged, necessitating reapplication of the instrument.

DR. KNAPP stated that he had watched some experiments several years ago to devise an apparatus whereby suction could be effected. The main difficulty proved to be the impossibility of shutting off the suction quickly enough. He believes that the large opening in the handle of Doctor McDannald's instrument would overcome this difficulty.

DR. M. J. LEVITT presented a patient with leprous keratitis of the superficial punctate type. S. R., 37 years old, suffered from keratitis punctata of the right eye in 1912; he was treated for 4½ months with K. I., atropine, yellow oxide, dionin, and regulation of diet, and made a complete recovery with $\frac{20}{15}$ vision. On June 15, 1920 he complained that the vision in the left eye had been blurred for two weeks. On examination there was slight ciliary congestion in the upper quadrant and to left of the cornea; there were numerous grayish-white dots and maculæ, some round, others irregular in shape, just beneath the epithelium, and a number of linear striæ; a network of minute, deep and superficial blood vessels resembling a brush, starting a little above the limbus and ending at the center of the cornea. At no time did the patient complain of pain or photophobia; vision was reduced to $\frac{20}{200}$ and the lower quadrant of the cornea was never involved.

The patient was born in Russia, came to New York 15 years ago, always lived in or around New York, was never exposed to leprosy; about 4½ years ago began complaining of itching about his left thigh and leg. On examination there was found present parasthesia of the left leg, thigh, and buttock; 8 to 10 brownish-red waxy-like nodules varying in size from a small pea to a ten cent piece; a few of these nodules were also present on the other leg and lower part of the trunk; he had alopecia of the eyebrows. A section taken from the lesion showed numerous lepra bacilli. Patient is now being treated at the Skin and Cancer Hospital with intermuscular injection of Heisler's

Mixture, a combination of chalmoogra oil, camphor oil, and resorcin. At present the skin condition is stationary and the parasthesia is somewhat improved. Under treatment with atropine, yellow oxide, dionin, and regulation of diet patient's vision improved from $\frac{20}{200}$ to $\frac{20}{40}$.

DOCTOR S. A. AGATSTON presented a patient with **tuberculosis choroiditis.**

Patient H. G., aged 55 years, came to the clinic at Bellevue Hospital with the complaint that ten days ago he noticed a sudden loss of vision in his right eye. Two months ago, he was brought to the psychopathic ward in a state of delirium and stupor. He remained in a stuporous state for three days. After that his mental condition was normal. His case was considered one of psychosis caused by arteriosclerosis. His blood pressure was 110—69. His heart was normal. His lungs, however, showed an extensive tuberculous process on both sides, and the patient has lost 25 pounds in weight during the past 8 months. His vision is: O. D. $\frac{20}{200}$, O. S. $\frac{20}{100}$. Ophthalmoscopic findings: O. D. vitreous opacities; a gray area in the region of the macula, 3 disks in diameter, raised about 1*mm* above the level of the retina. The border of the area was diffuse, light-colored retinal blood vessels passing over the area. O. S. vitreous opacities, and two similar areas in the lower portion of the fundus.

The Wassermann test was negative; the patient has very bad teeth.

DOCTOR C. E. MCDANNALD presented a patient with **keratectasia.**

DISCUSSION: DOCTOR CLAIBORNE asked if Dr. McDannald had examined the case with Placido's disk. A moment's use of Placido's disk would reveal whether this case was one of keratectasia or simply keratoglobus. He stated he found Placido's disk of great value in finding astigmatism and used it frequently in place of the ophthalmometer. A strong lens held behind the disk would give a corneal image so that the astigmatism or its absence could be detected at once. When there is no astigmatism the image of the disk on the cornea is circular, when there is, it is elliptical. In astigmatism with the rule, the long axis of the ellipse lies along the horizontal, against the rule lies vertical; in oblique astigmatism it is oblique. He

found it possible not only to diagnose the astigmatism but to come within ½ to 1 D. of the amount and the axis within 5 to 10 degrees. Dr. Claiborne desired to recall the value of this method of examination, which had fallen into disuse, to those young men who had never used it and also to the older men who had used it and laid it aside. He had used it during the recent war in examining men for malingering. It was a great time saver.

Doctor George Vandegrift believes this to be a congenital anomaly as the woman has had the condition since birth. He thinks it is a reversion to the animal type of cornea for it is similar to the corneæ of fish.

Doctor Arnold Knapp said that he believed this to be a case of marginal corneal degeneration and called Doctor McDannald's attention to the scarred periphery of the cornea.

The paper of the evening was read by Doctor Alfred Wiener and Doctor Ellis Bonime on **sympathetic ophthalmia**—report of a case successfully treated. Doctor A. Wiener discussed the surgical treatment and Doctor Bonime, immunotherapy. (Complete paper appears in this issue.)

Discussion: Doctor E. S. Thomson said that this had evidently been a severe type of the disease and shows that surgical intervention is disastrous unless the inflammatory process is controlled before operation. The result certainly seemed a very good one.

Doctor Colman W. Cutler said: This is an extremely interesting and valuable contribution. The gravity of the condition, the apparently hopeless prognosis was obvious. There were probably foci of infection in the uveal tract which may in the long course of time have become attenuated, but by the repeated recurrences the eyes had become so sensitive that without the most thorough reinforcement of resistance or immunization and perhaps sterilization (for that is a fair statement), no further operative steps would have been feasible. The picture was that of a proliferative uveitis. The trend of opinion as to the etiology of sympathetic ophthalmia is toward an infection by an undiscovered organism. The cytotoxin theory and that of uveal anaphylaxis are still held, and the anaphylaxis of uveal pigment possibly influenced by a protein poison of bacillus prodigiosus is supported by Dr. Alan Wood's recent

interesting work which seems the most valuable yet done in this field. It is not possible to summarize the work here, but it deserves very careful consideration. In any case the normal resistance of the eye may be so lowered that streptococci or staphylococci from neighboring or distant foci may lodge in the uveal tissues and the familiar picture of uveitis ensue, complicating the original plastic or proliferative uveitis of sympathetic origin. This might account for the success of the immunizing treatment in this case and justify its application in similar cases. Such complications probably offer a more hopeful field for vaccine or serum treatment than a disease due to a protein poison apart from the actual bacteria if such exists. In a case under observation, the right eye developed uveitis twenty years ago, became blind and glaucomatous and was enucleated in 1915 because of pain, after an iridectomy had failed to give relief. The remaining eye became affected probably before the iridectomy and for five years a chronic iridocyclitis has existed in spite of every effort to find and eliminate a focus. The eye has apparently been benefited—I may say saved, so far—by streptococcus vaccine given by Dr. John Richards. Syphilis and gonococcus infection were proven absent, but recently a noticeable improvement has followed treatment of the deep urethra by Dr. Lowsley and the use of a streptococcus vaccine from that region. I shall hope to report the case in detail later; it shows the necessity of persistence in the search for a hidden focus. In this case the teeth, tonsils, accessory sinuses, have been literally eliminated, and the possible source of his trouble is a prostate that gave no sign of disease until vigorously explored and treated. It is of vital importance in this case, as in Dr. Wiener's, to put the eye at rest, as a cataract is developing and the question of operation on an eye with uveitis must be faced.

Few chronic inflammations are simple; the lowered vitality of the tissues and the probable mixed infection should encourage the use of any measures not harmful, and such a case as this of Dr. Wiener's may well induce an optimism not hitherto felt.

Dr. Knapp doubted the diagnosis of sympathetic ophthalmia in this case because he thought it very unusual for the second eye to become affected when the first eye, instead of showing an aggravation of its symptoms, was steadily im-

proving. He wanted to ask whether in the last operation the iris had been attacked, because it is a matter of experience that these eyes will stand an operation on the capsule but not one on the iris. He also would like to ask whether the injection of foreign proteid was regularly followed by any change in the symptoms of the eyes.

Doctor Ben Witt Key said that he had confidence in the effect of foreign protein whether bacterial (pneumococci or diphtheria) or other protein, injected to combat ocular infection, for his experience with the injection of anti-diphtheritic serum in severe ocular infection showed definite results almost every few days at the New York Eye and Ear Infirmary. However, he hesitated to accept the case reported as one of sympathetic ophthalmia, especially when mindful of a case in the hospital now with recurrent attacks of plastic iridocyclitis, having improved from $\frac{20}{200}$ to $\frac{20}{20}$ vision during four distinct periods of time after injections of tuberculin, and though the process followed upon an injury and removal of the fellow eye and clinically appeared to be one of sympathetic ophthalmia.

Doctor A. E. Davis asked why Doctor Bonime used typhoid vaccine in preferrence to other proteins.

Doctor Wiener in closing said that he thought this to be a true case of sympathetic ophthalmia and replying to Doctor Knapp said that while previous to the immuno-therapy, the slightest interference with the iris brought on an attack of iridocyclitis, after the above treatment no reaction occurred. In reply to the question whether the injection of protein brought on any irritation, Doctor Wiener stated that first all the symptoms of the existing low grade iridocyclitis were intensified, but gradually disappeared as the treatment was carried out.

Doctor Bonime in closing said that he used typhoid vaccines because the dosage was so easily regulated and there is no danger in the use of a foreign serum like diphtheria antitoxin. He used the pneumococcus and streptococcus in connection with the typhoid, his aim being to obtain results. For the future he suggests that the cases be treated in series, some with streptococcus, some with pneumococcus, and some with typhoid alone, in order to determine which was the effective vaccine, or whether, after all, the combination was necessary to bring about the results.